



QUANTITATIVE

NON-TARGETED SCREENING

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We do not describe the world
we see, we see the world we can
describe.

~ Rene Descartes

AZ QUOTES

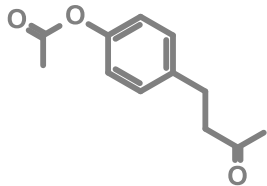
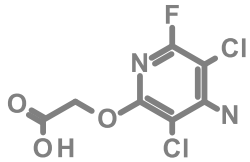
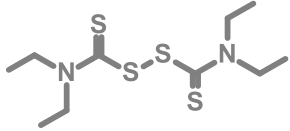
To monitor the health of cities' residents, look no further than their sewers
C&EN 96 (2018)





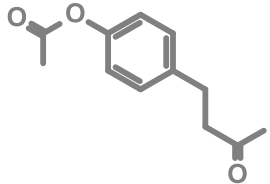
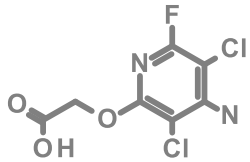
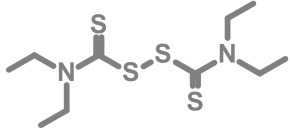
BACKGROUND OF NON-TARGETED SCREENING

FROM TARGETED TO NON-TARGETED

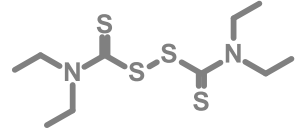


FROM TARGETED TO NON-TARGETED

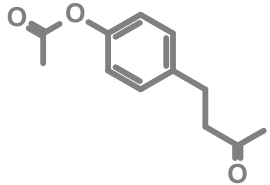
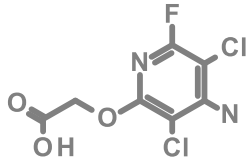
MRM MODE



FROM TARGETED TO NON-TARGETED

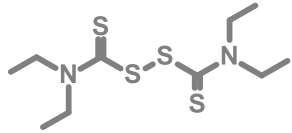


MRM MODE

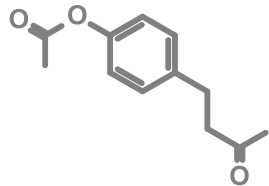
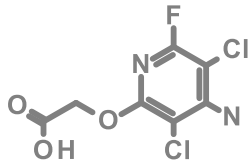


NO TARGETED LIST

FROM TARGETED TO NON-TARGETED

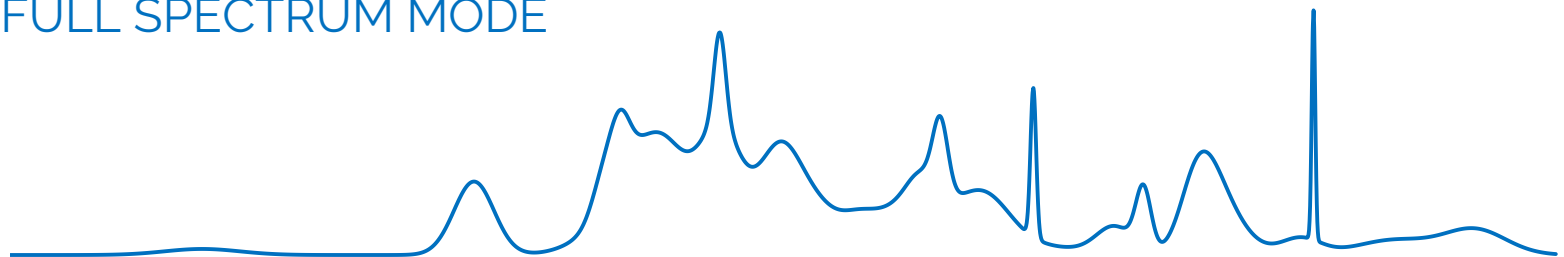


MRM MODE



NO TARGETED LIST

FULL SPECTRUM MODE



A serene landscape featuring a small, leafy tree growing out of a moss-covered rock in the middle of a calm lake. The water reflects the surrounding greenery and the sky. In the background, a dense forest of tall trees lines the shore. The overall atmosphere is peaceful and natural.

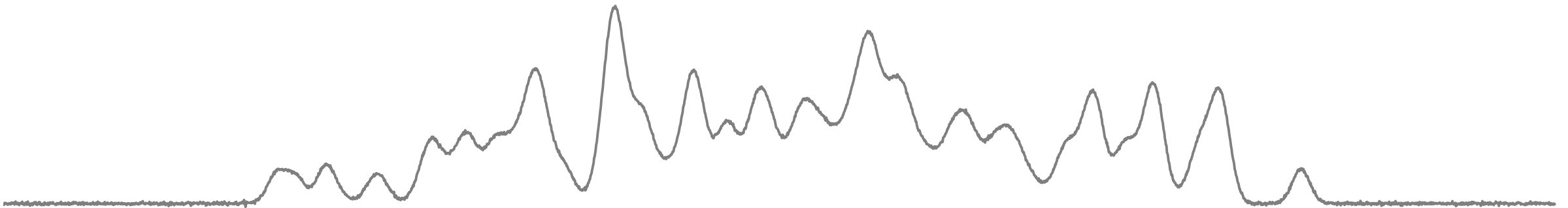
SCREENING OF SURFACE WATER IN COLLABORATION WITH KWR

SAMPLES

SURFACE WATER FROM THE NETHERLANDS

28 different locations

FULL SPECTRUM MODE



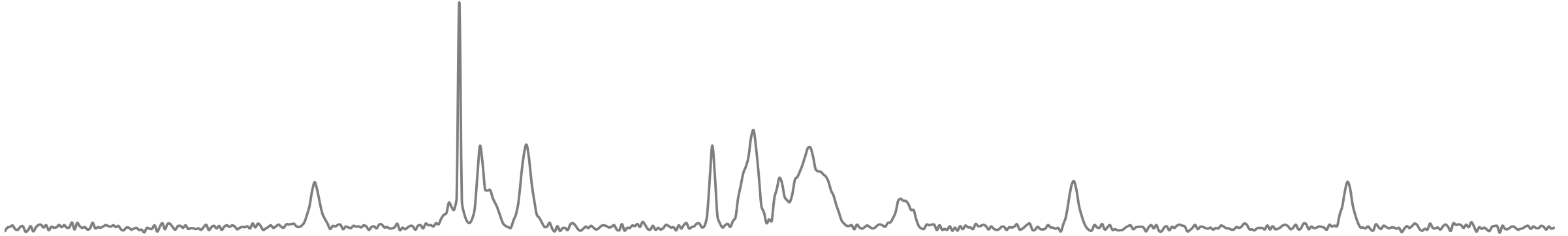
Anneli Kruve

SAMPLES

SURFACE WATER FROM THE NETHERLANDS

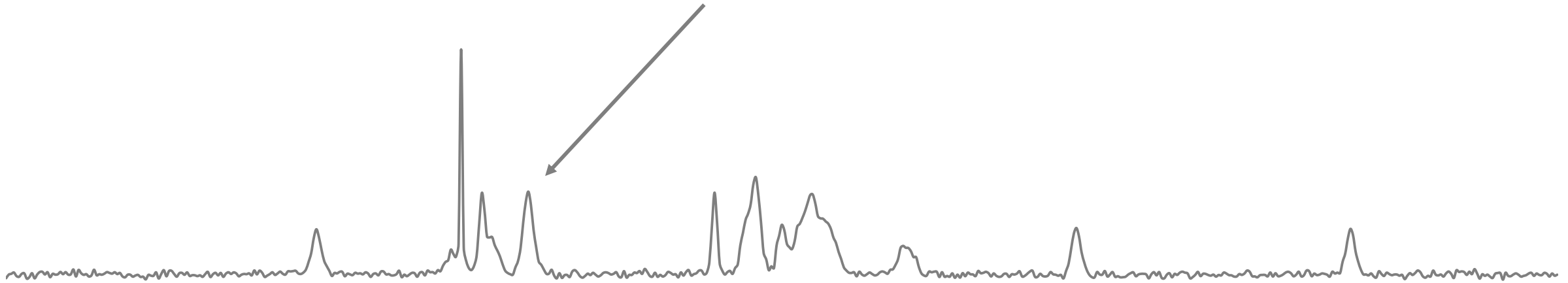
28 different locations & 119 different peaks

FULL SPECTRUM MODE



IDENTIFICATION

$t_R = 10.1$ min



IDENTIFICATION

$t_R = 10.1\text{ min}$

133.0640

Level 5: Exact mass of interest	MS
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IDENTIFICATION

$t_R = 10.1$ min

$C_7H_7N_3$

Level 4: Unequivocal molecular
formula

MS isotope/adduct

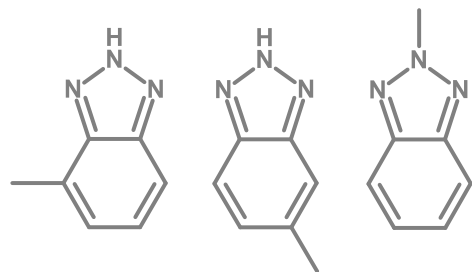
133.0640

Level 5: Exact mass of interest

MS

IDENTIFICATION

$t_R = 10.1$ min



$C_7H_7N_3$

133.0640

Level 3: Tentative candidate(s)
structure, substituent, class

MS, MS², Exp. data

Level 4: Unequivocal molecular
formula

MS isotope/adduct

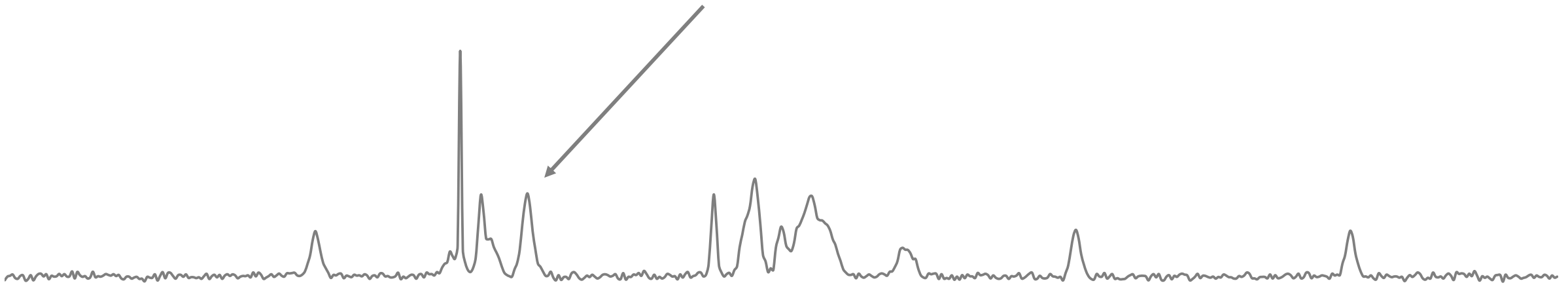
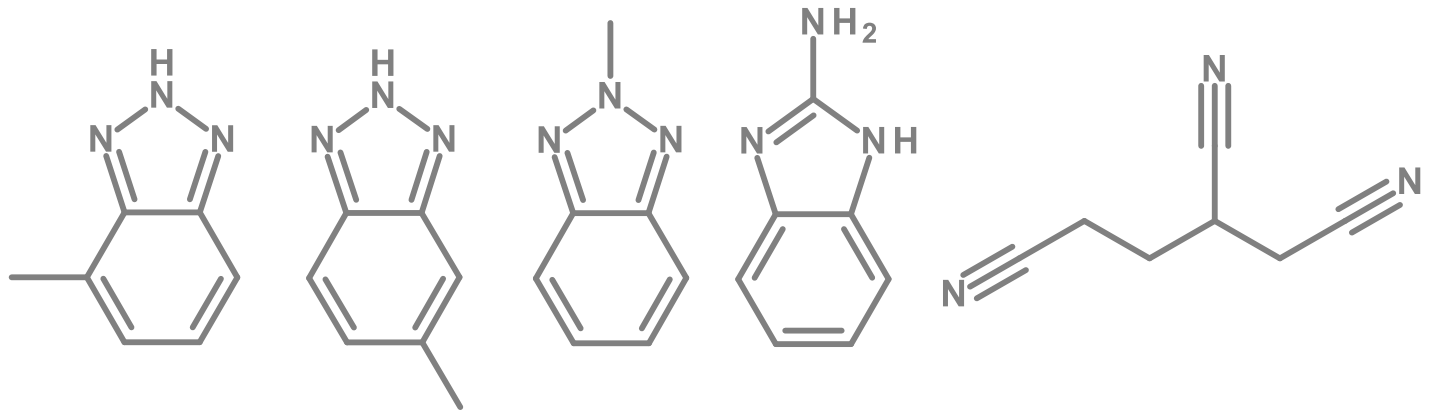
Level 5: Exact mass of interest

MS

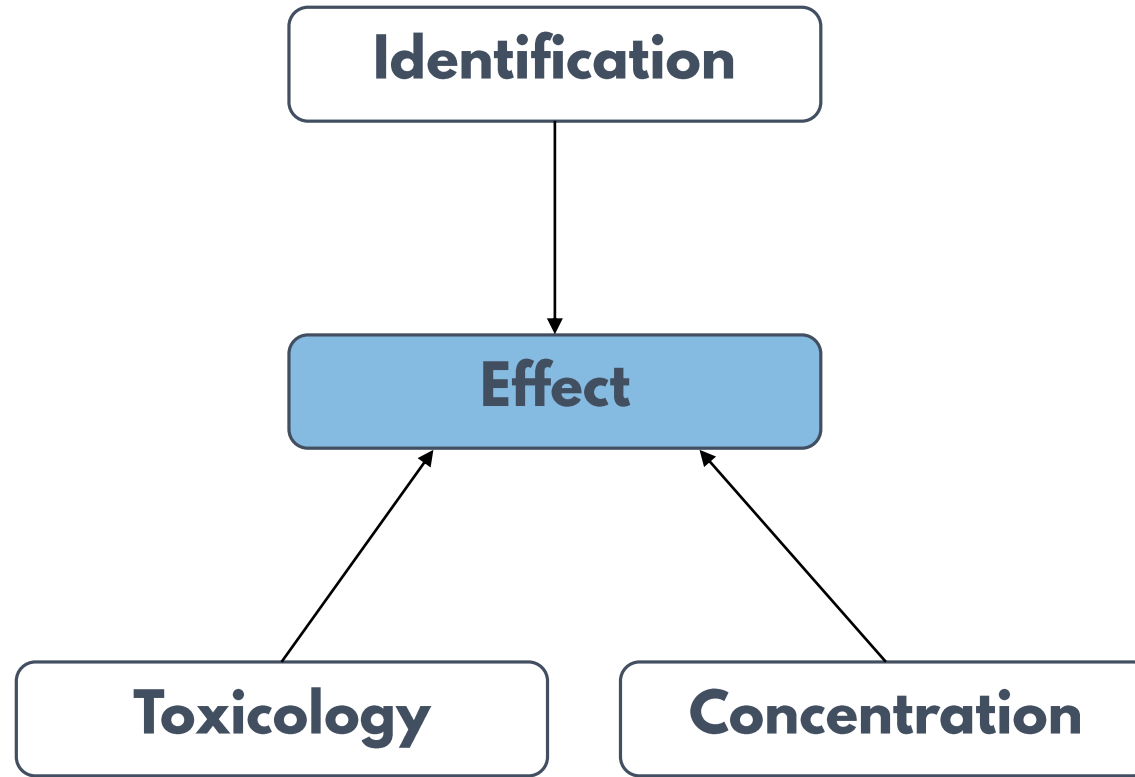
IDENTIFICATION

$t_R = 10.1$ min

5 possible structures



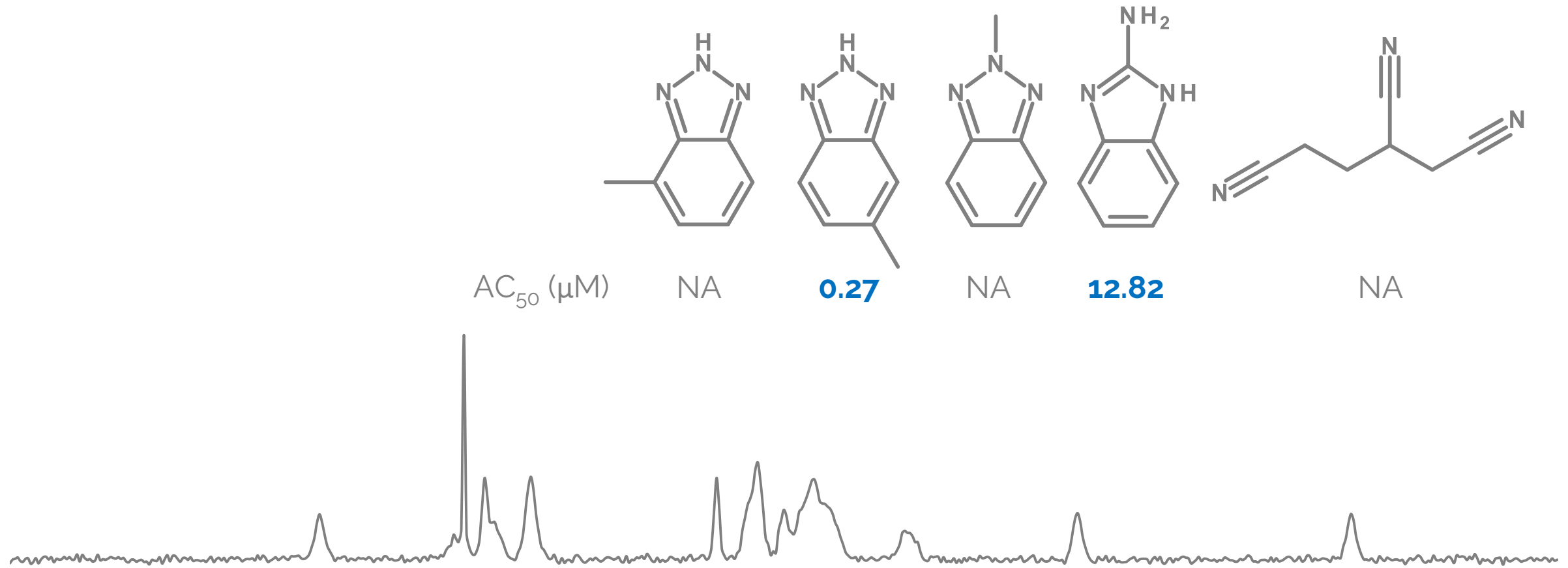
EFFECT DRIVEN INTERPRETATION



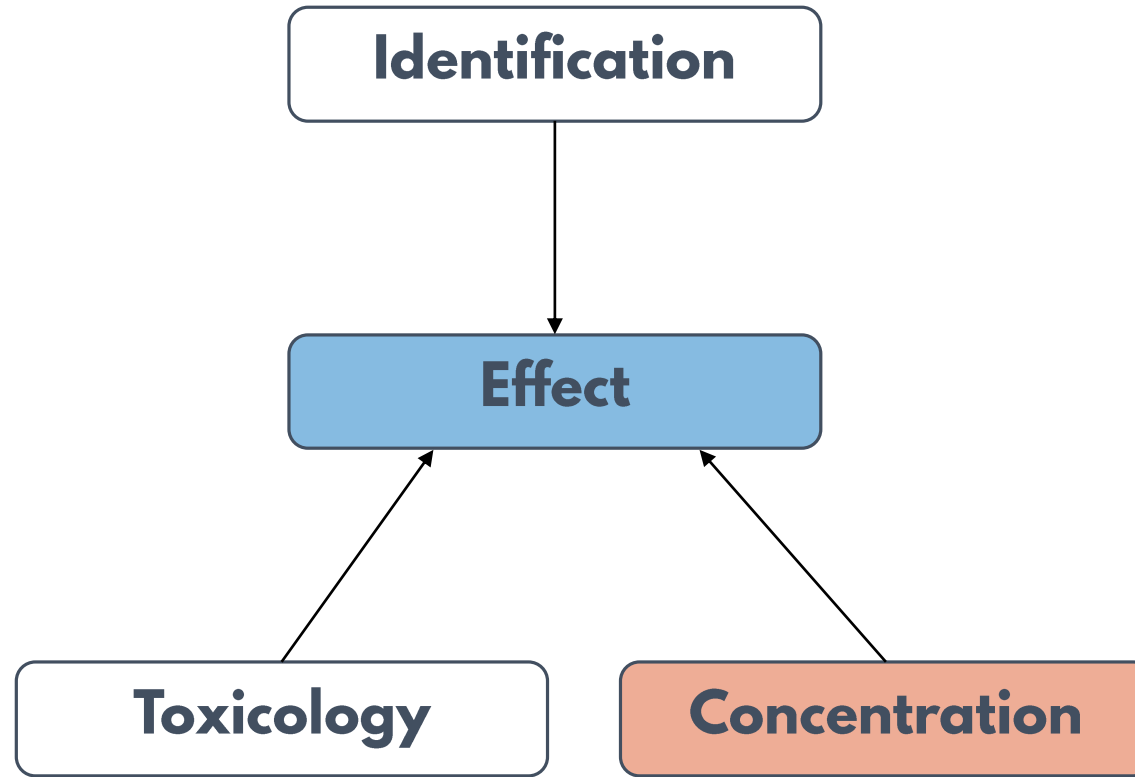
PRIORITIZATION

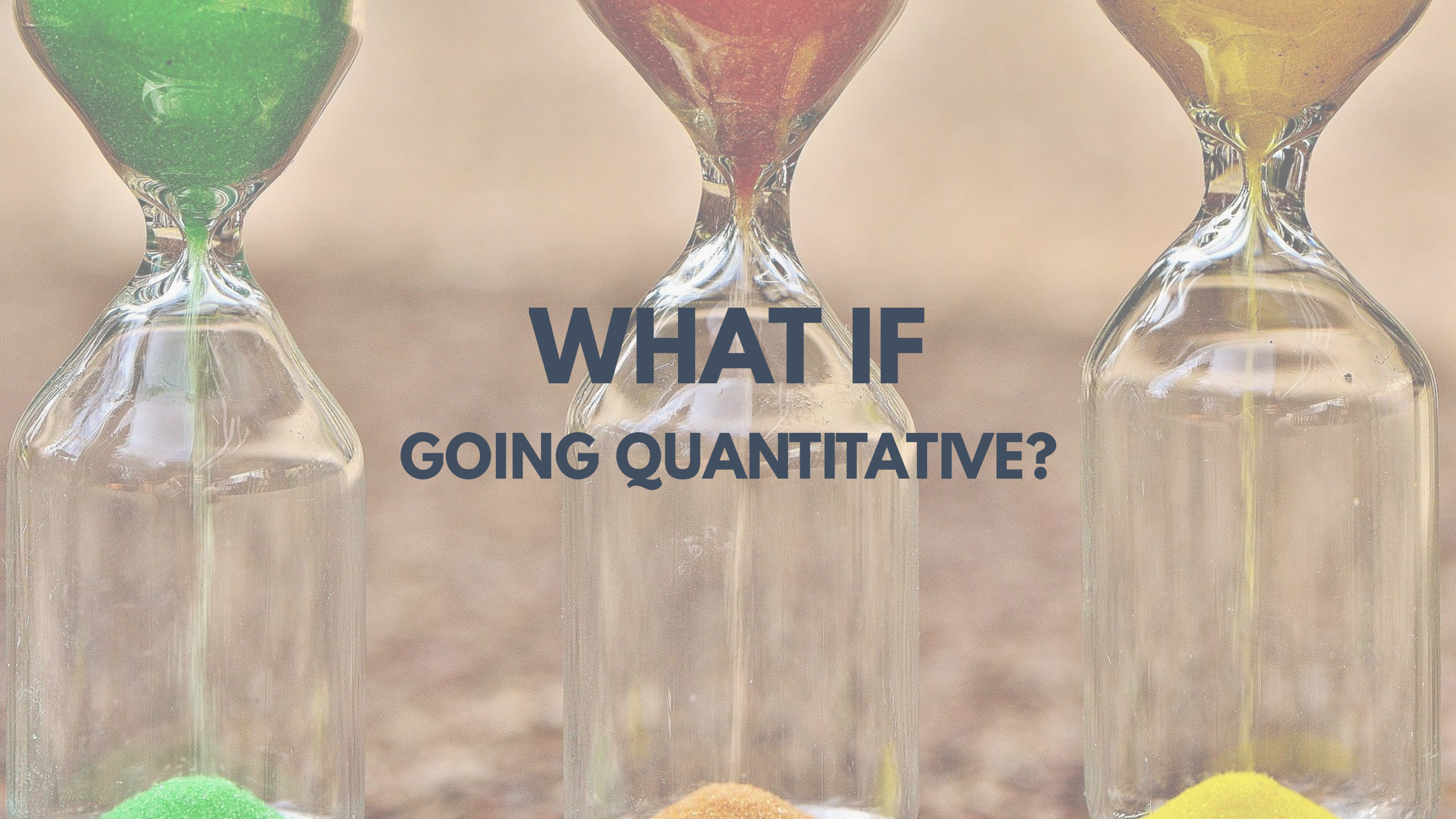
BASED ON TOXICITY

ToxCast toxicity tests



EFFECT DRIVEN INTERPRETATION



Three glass hourglasses are shown side-by-side. The left one contains green sand, the middle one red sand, and the right one yellow sand. In each, the top bulb is full and the bottom bulb contains a small pile of the same colored sand, with a stream of sand falling from the neck. The background is a soft, out-of-focus brown.

**WHAT IF
GOING QUANTITATIVE?**

QUALITATIVE

stop after identification

QUANTITATIVE

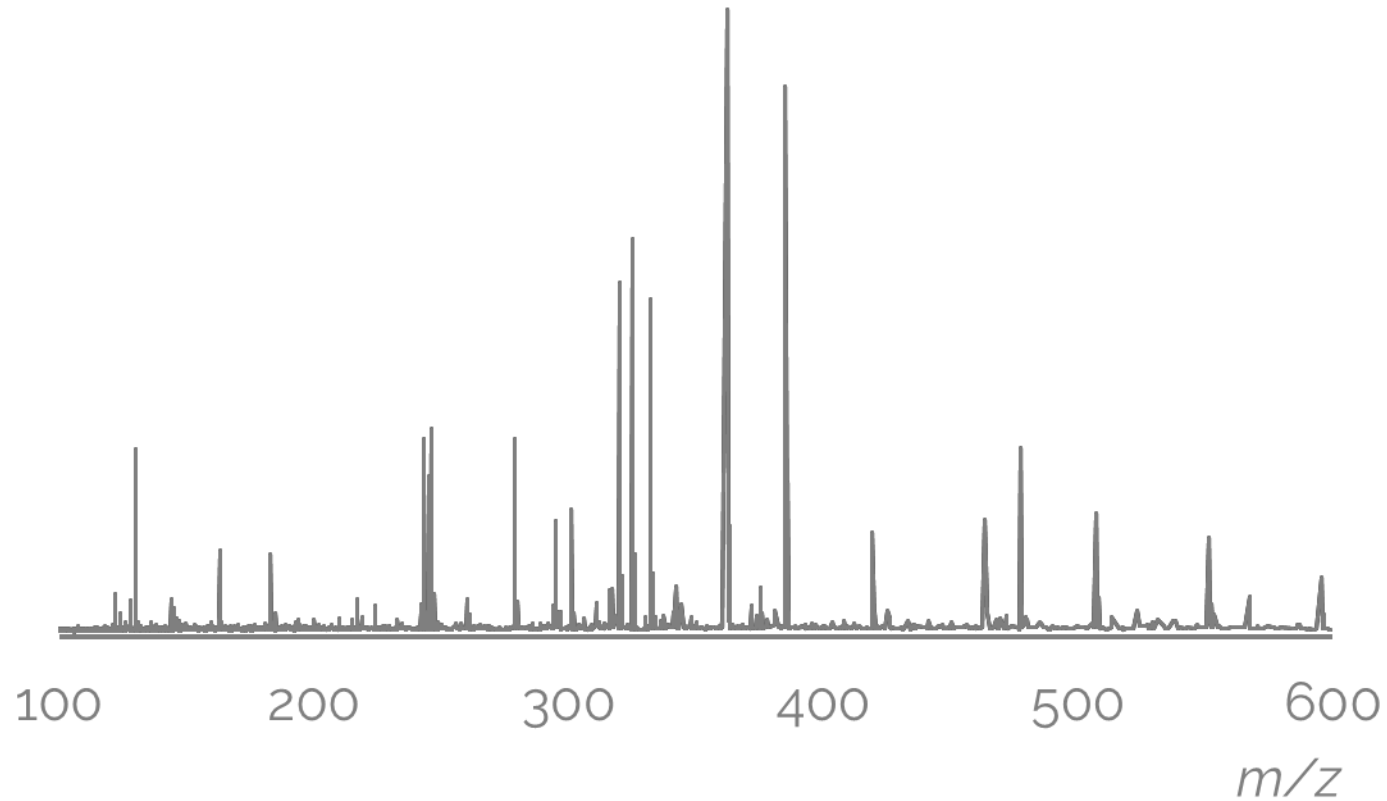
purchase or synthesize the standard substances



QUANTIFICATION IS COMPLICATED

ESI/HRMS NON-TARGETED ANALYSIS

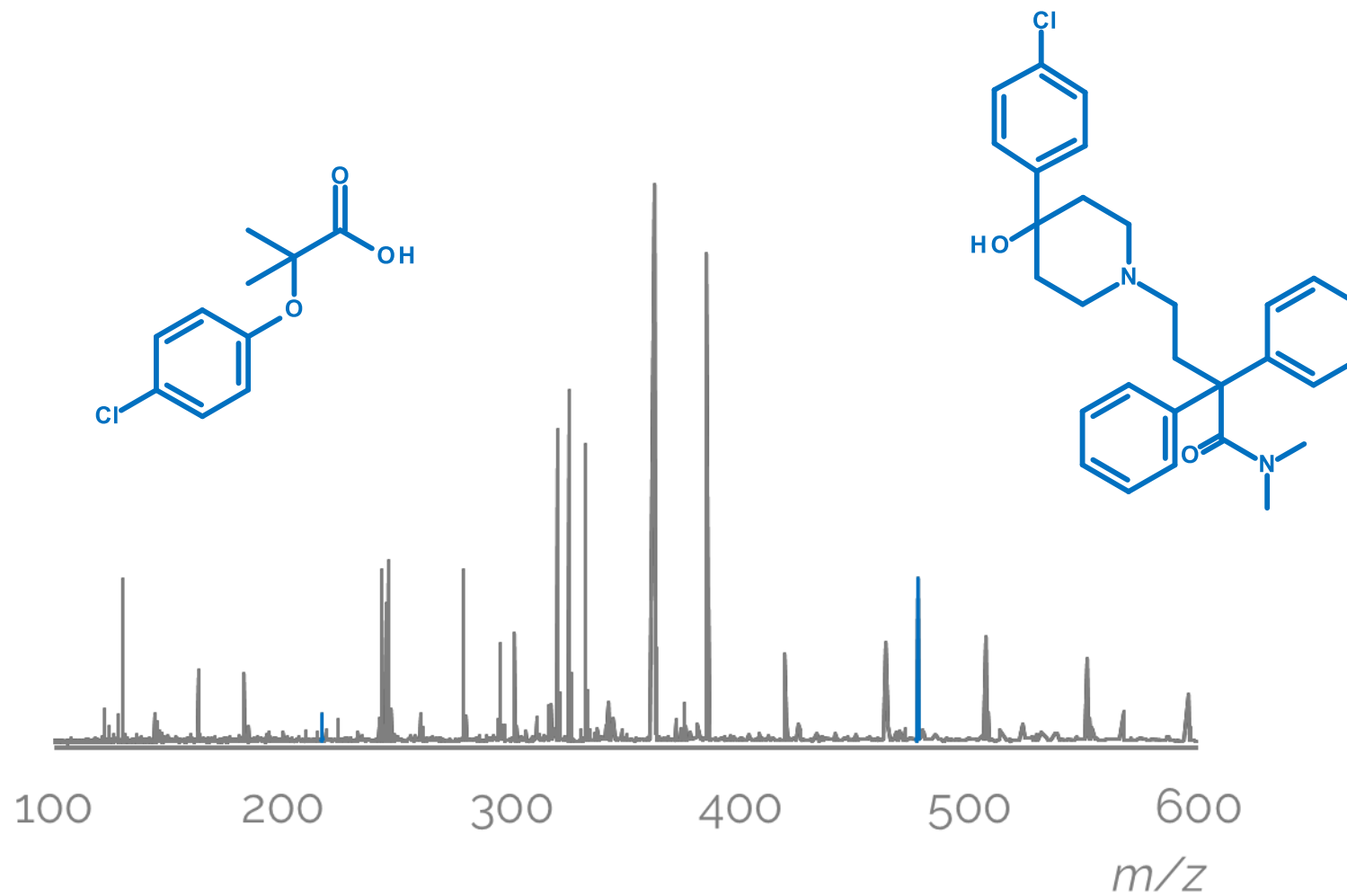
reveals hundreds of compounds



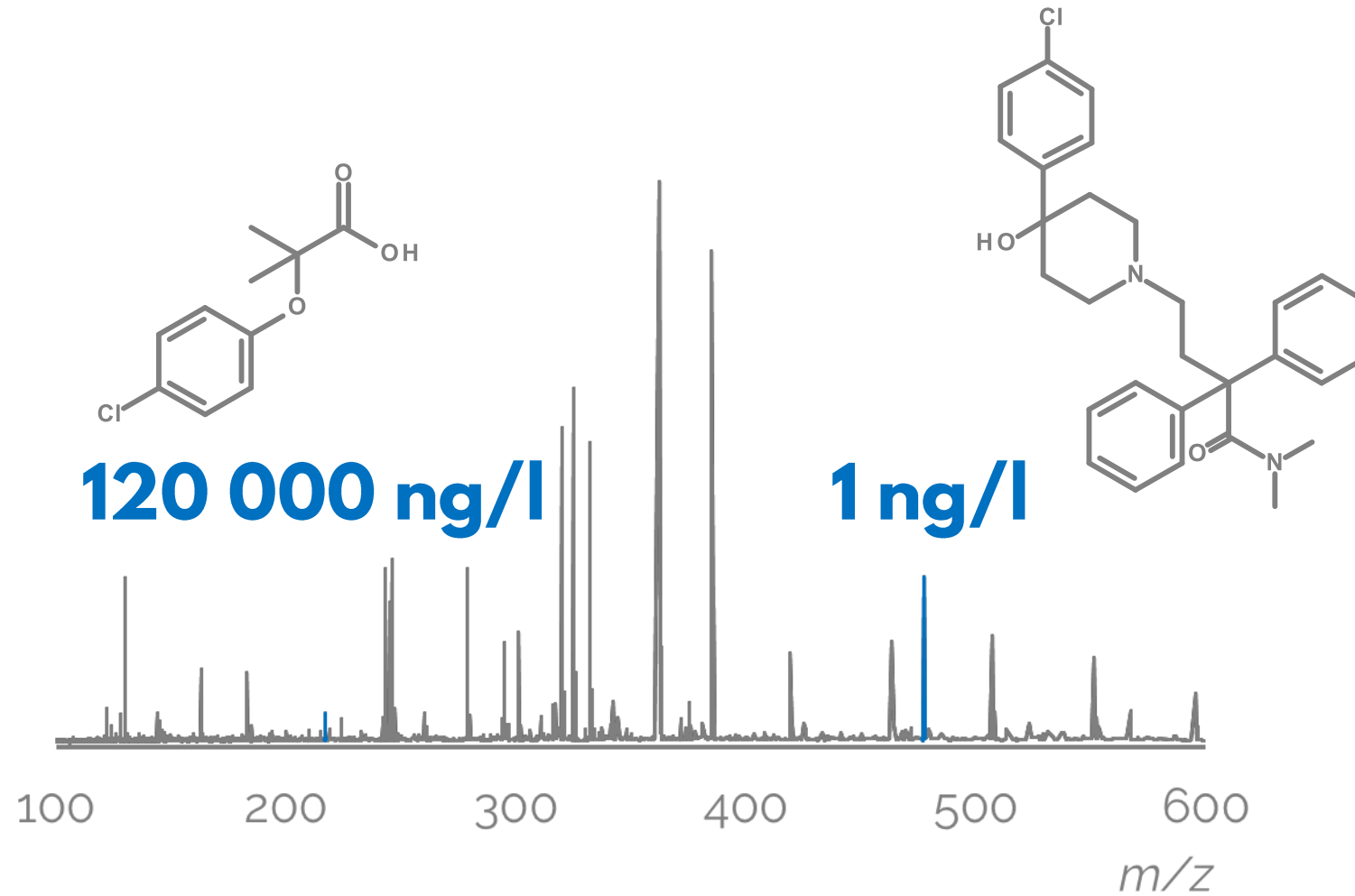
QUANTIFICATION IS COMPLICATED

ESI/HRMS NON-TARGETED ANALYSIS

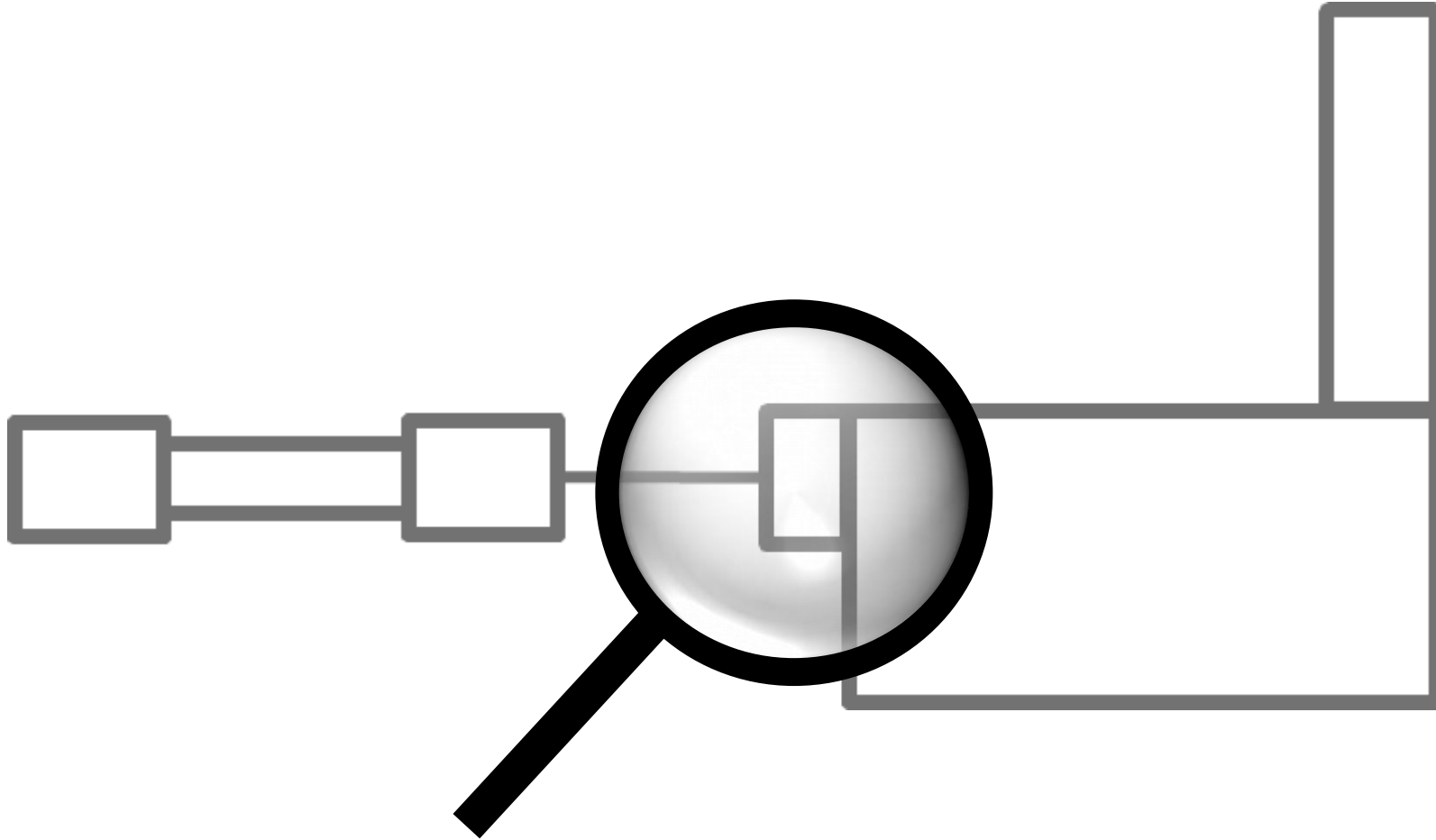
reveals hundreds of compounds

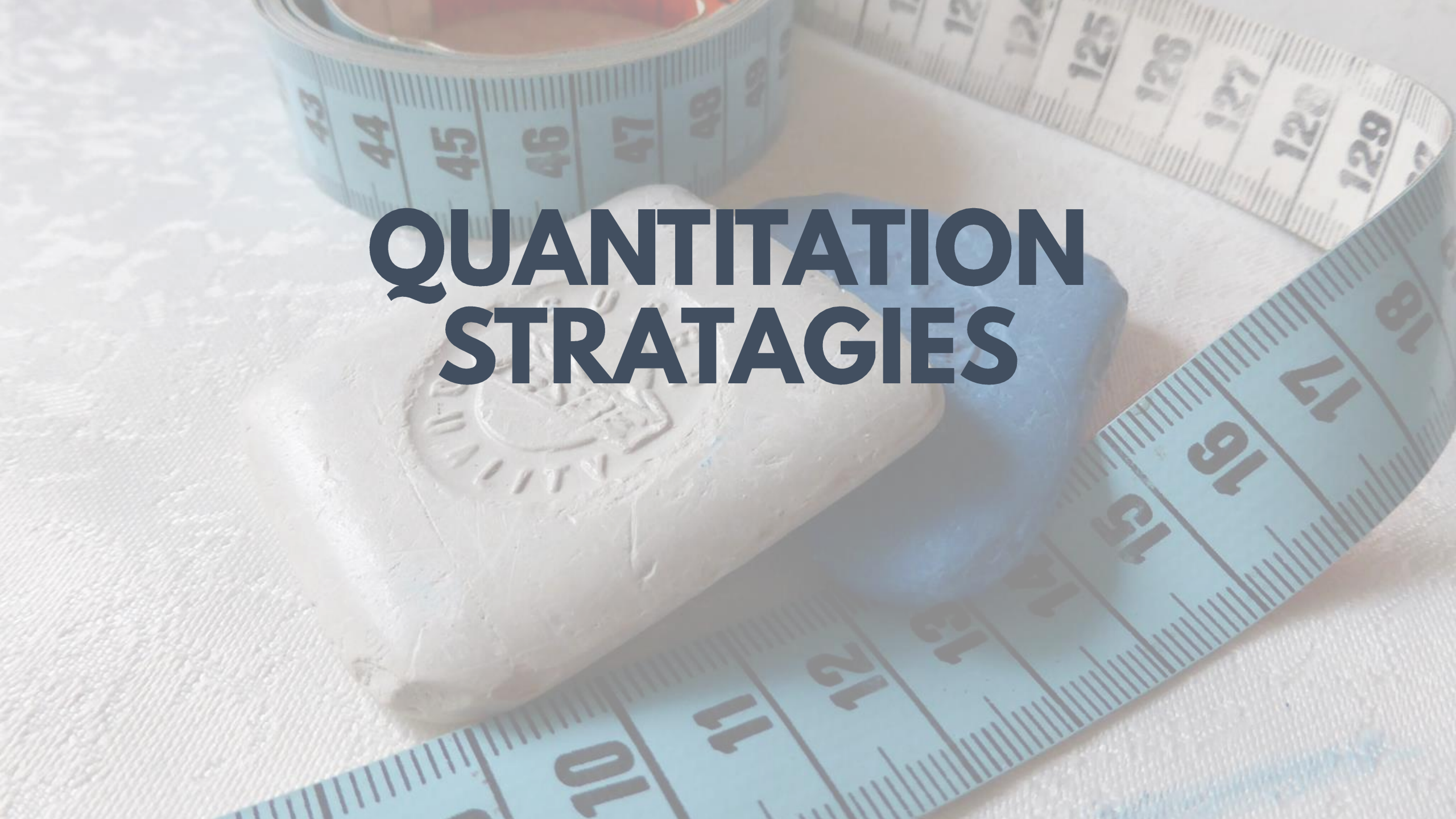


SO WHAT IS THE CONCENTRATION?



ELECTROSPRAY IONIZATION PROCESS



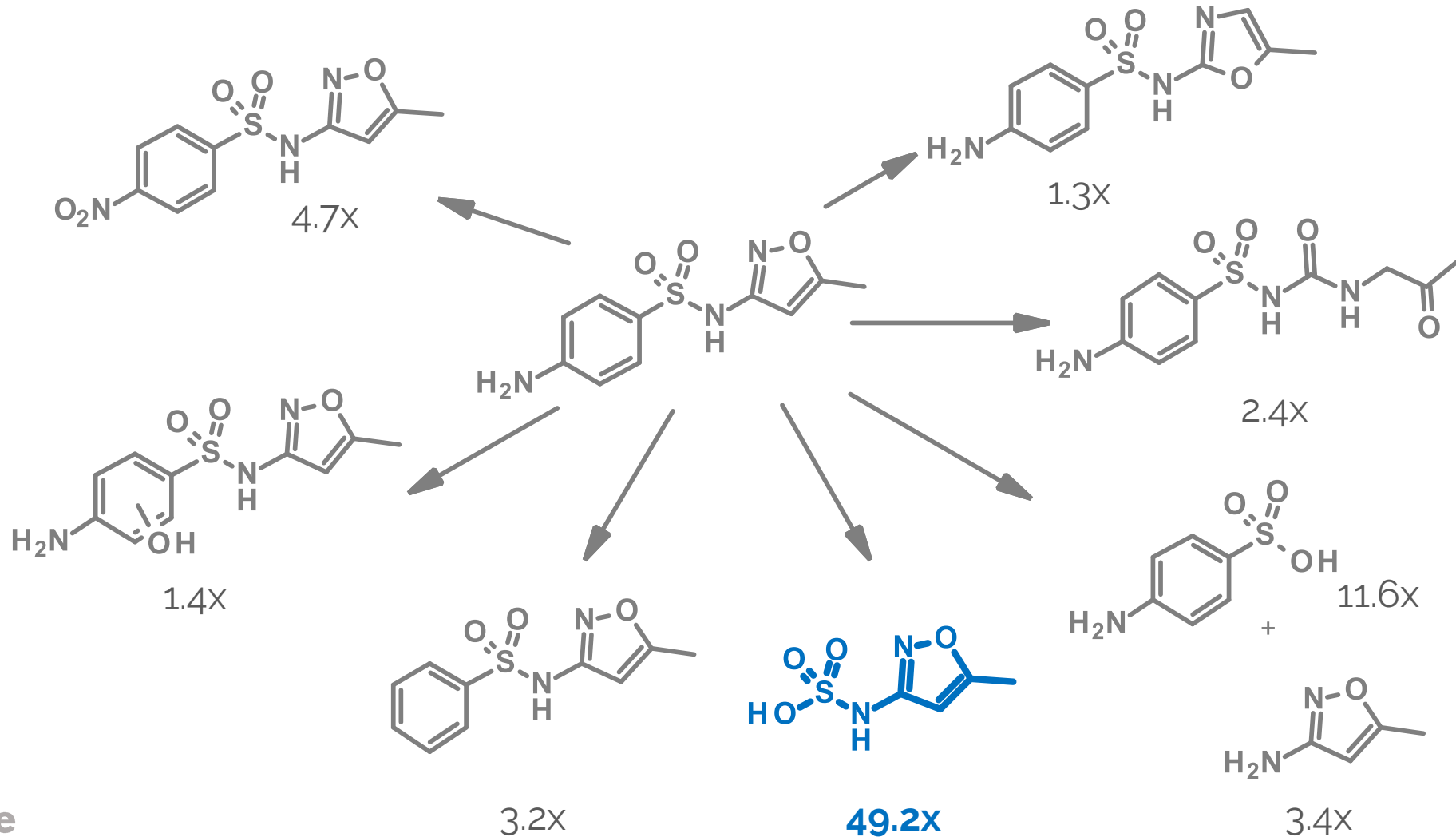


QUANTITATION STRATEGIES

PARENT COMPOUND

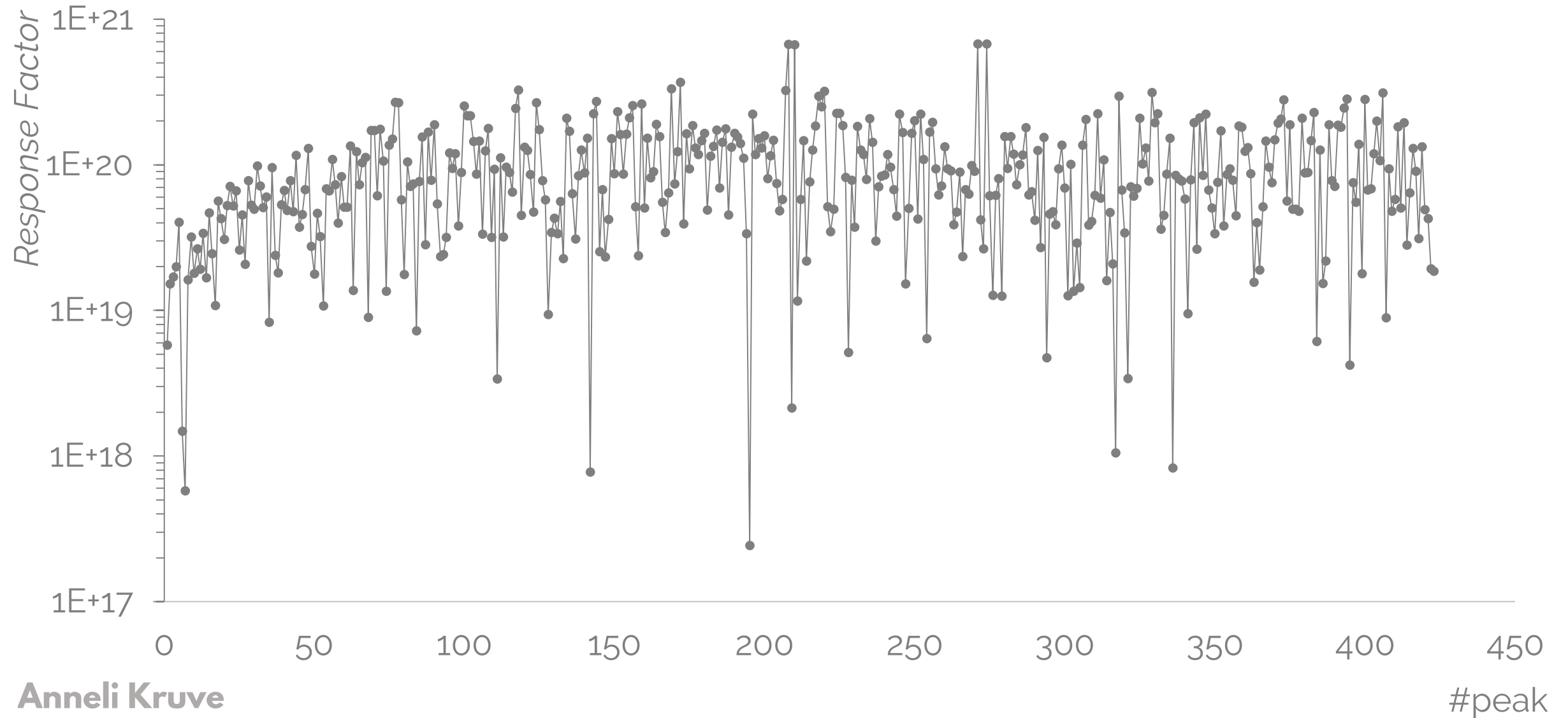
FOR CALIBRATION

up to 50 times lower ionization efficiencies relative to parent drug



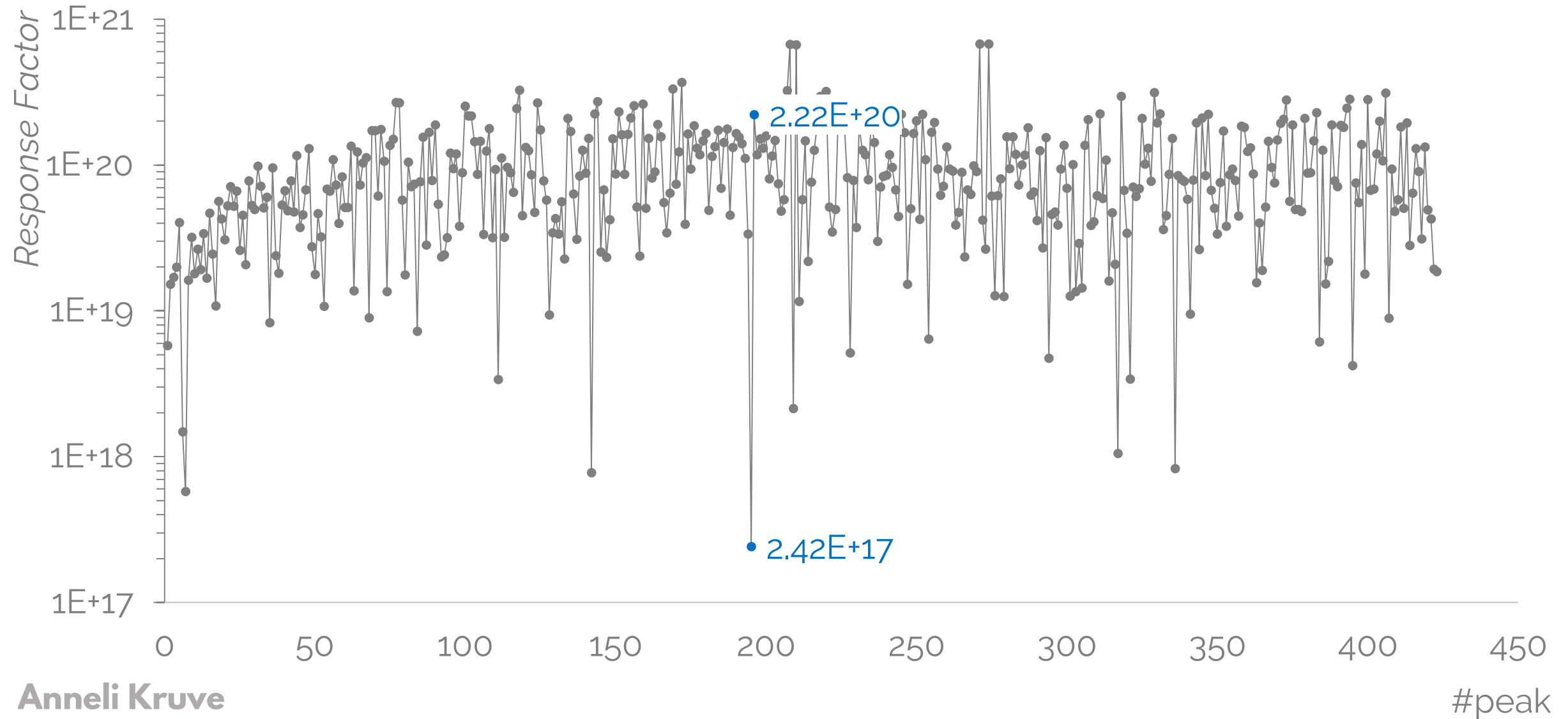
COMPOUND ELUTING CLOSEST

TO THE COMPOUND OF INTEREST



COMPOUND ELUTING CLOSEST

TO THE COMPOUND OF INTEREST



A high-speed, close-up photograph of water splashing, creating numerous droplets and bubbles. The water is clear and bright, with some droplets in sharp focus while others are blurred in the background, creating a sense of motion and depth. The overall tone is cool and scientific.

IONIZATION EFFICIENCY

FOR ESI SOURCE

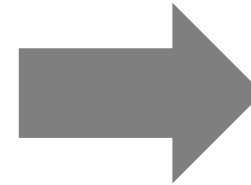
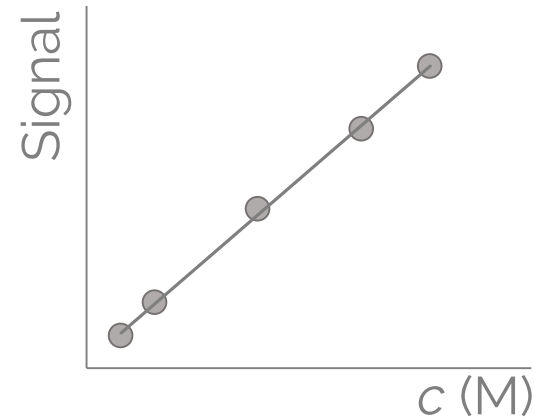
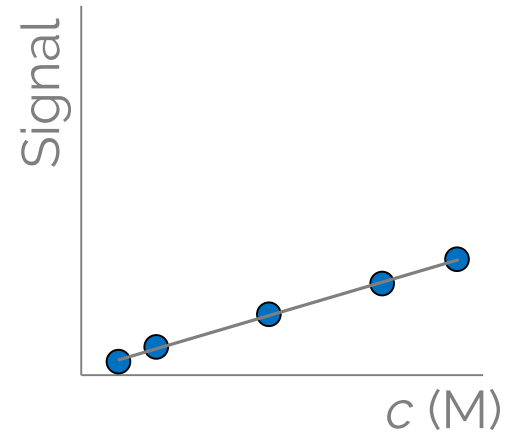
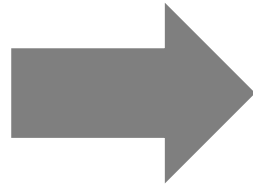
IONIZATION EFFICIENCY

RELATIVE MEASUREMENTS

flow injections

calibration graph

calculation



$$\frac{\text{slope}_1}{\text{slope}_2} \rightarrow IE$$

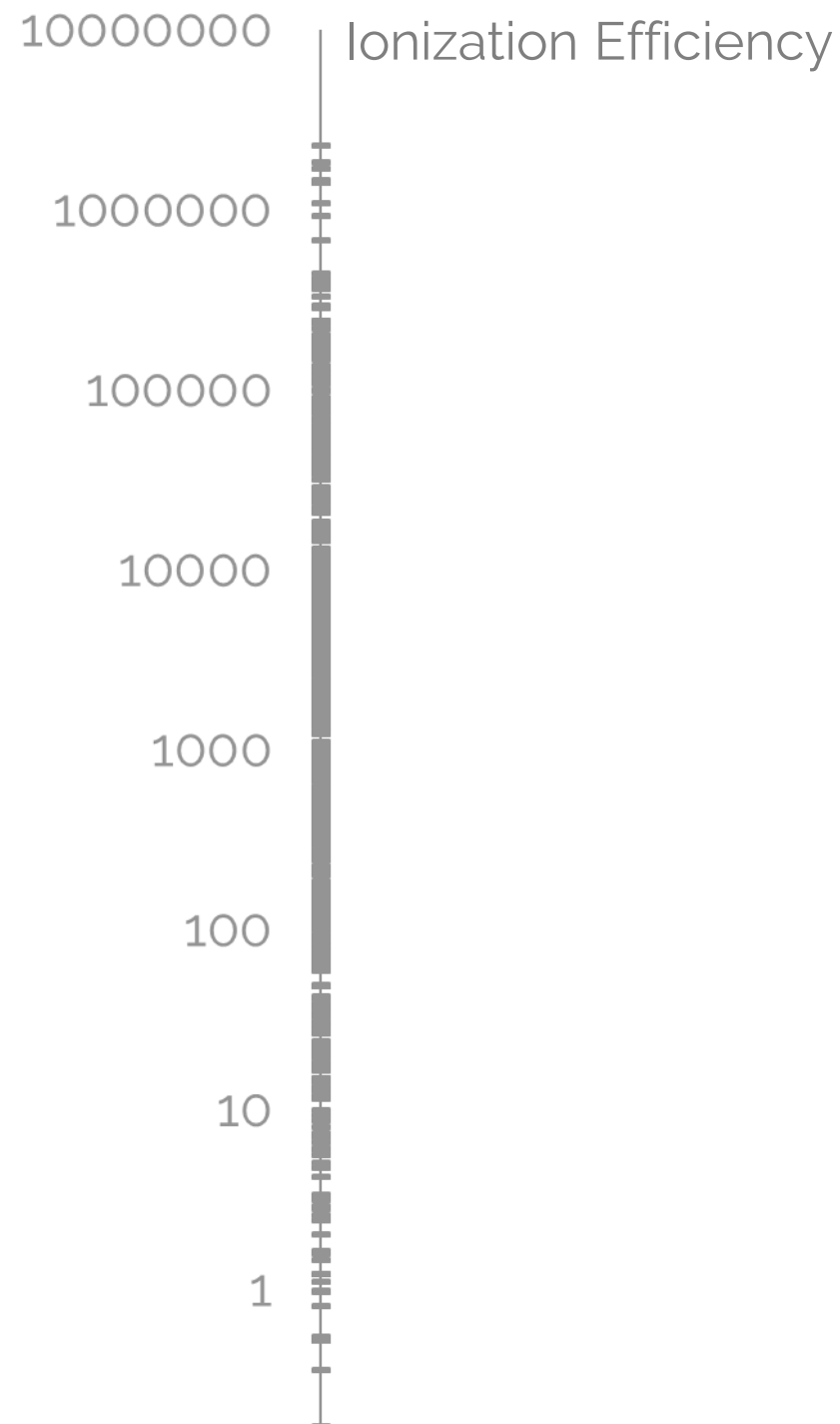
IONIZATION EFFICIENCY

IS AFFECTED BY



STRUCTURE

INTERPLAY BETWEEN PROPERTIES

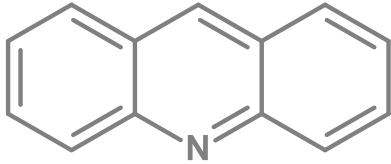


STRUCTURE

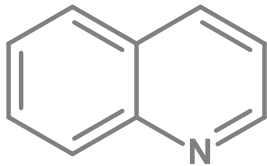
INTERPLAY BETWEEN PROPERTIES

$\log P$

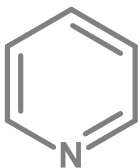
3.40



2.03



0.65



10000000

1000000

100000

10000

1000

100

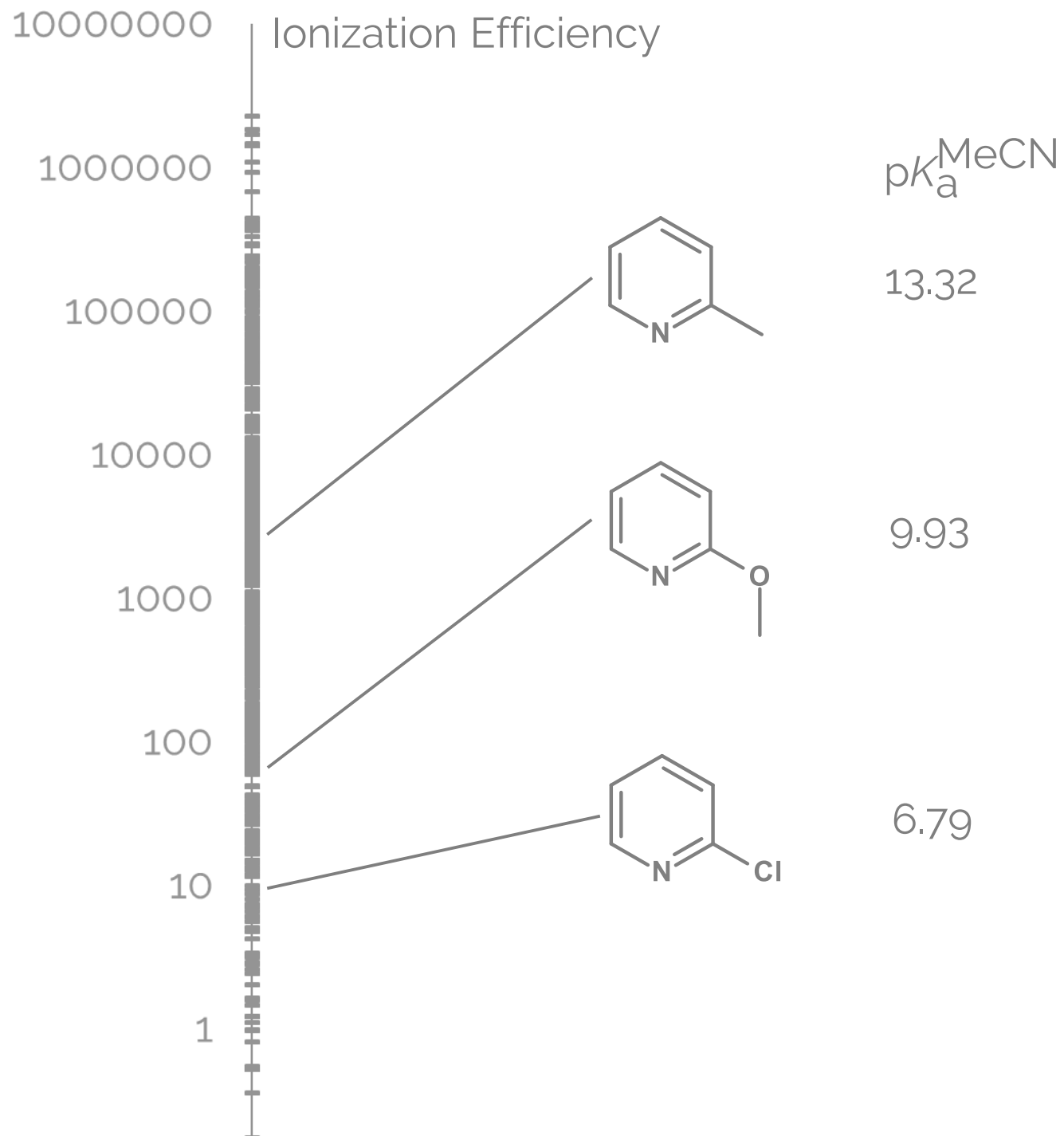
10

1

Ionization Efficiency

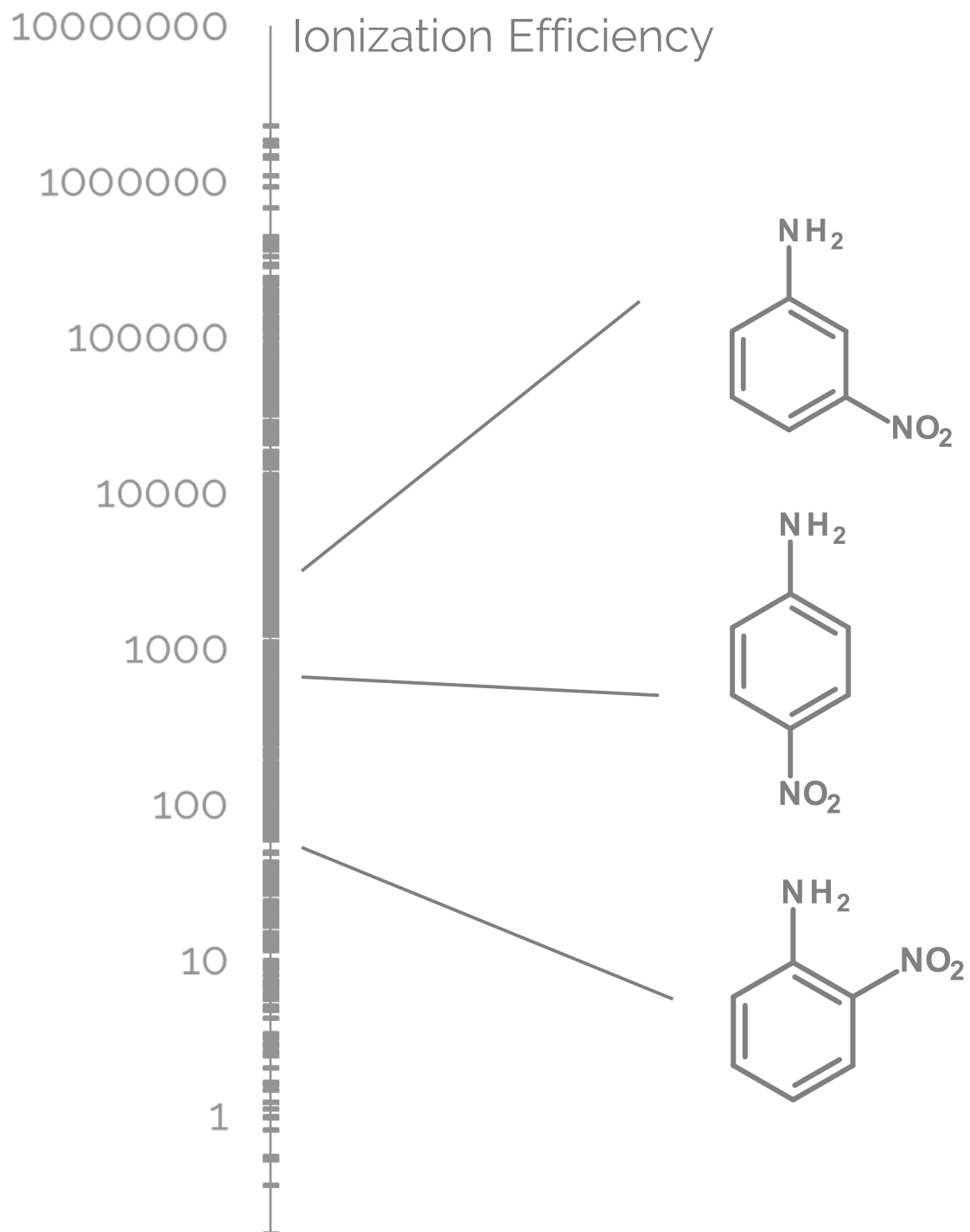
STRUCTURE

INTERPLAY BETWEEN PROPERTIES



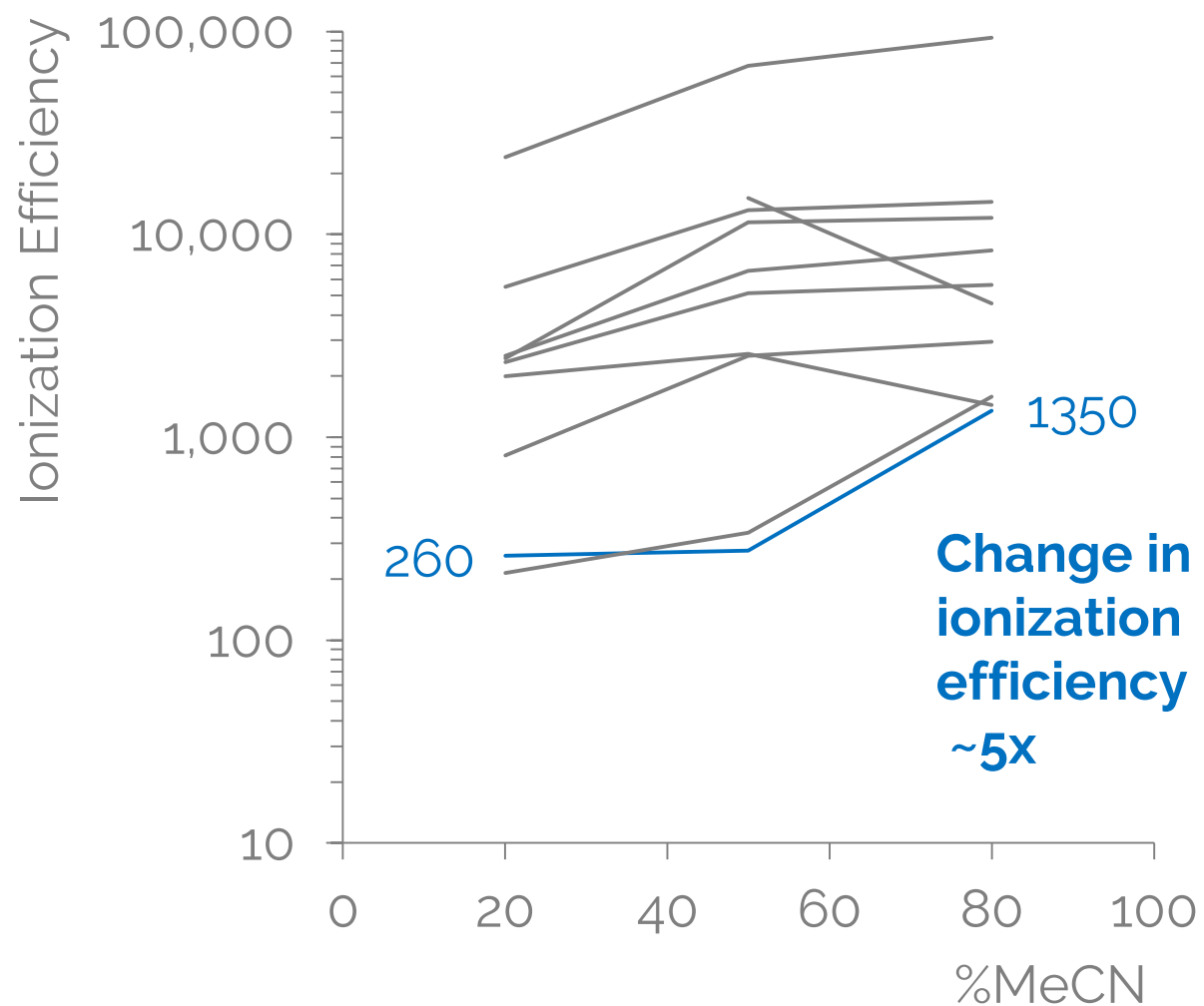
STRUCTURE

INTERPLAY BETWEEN PROPERTIES



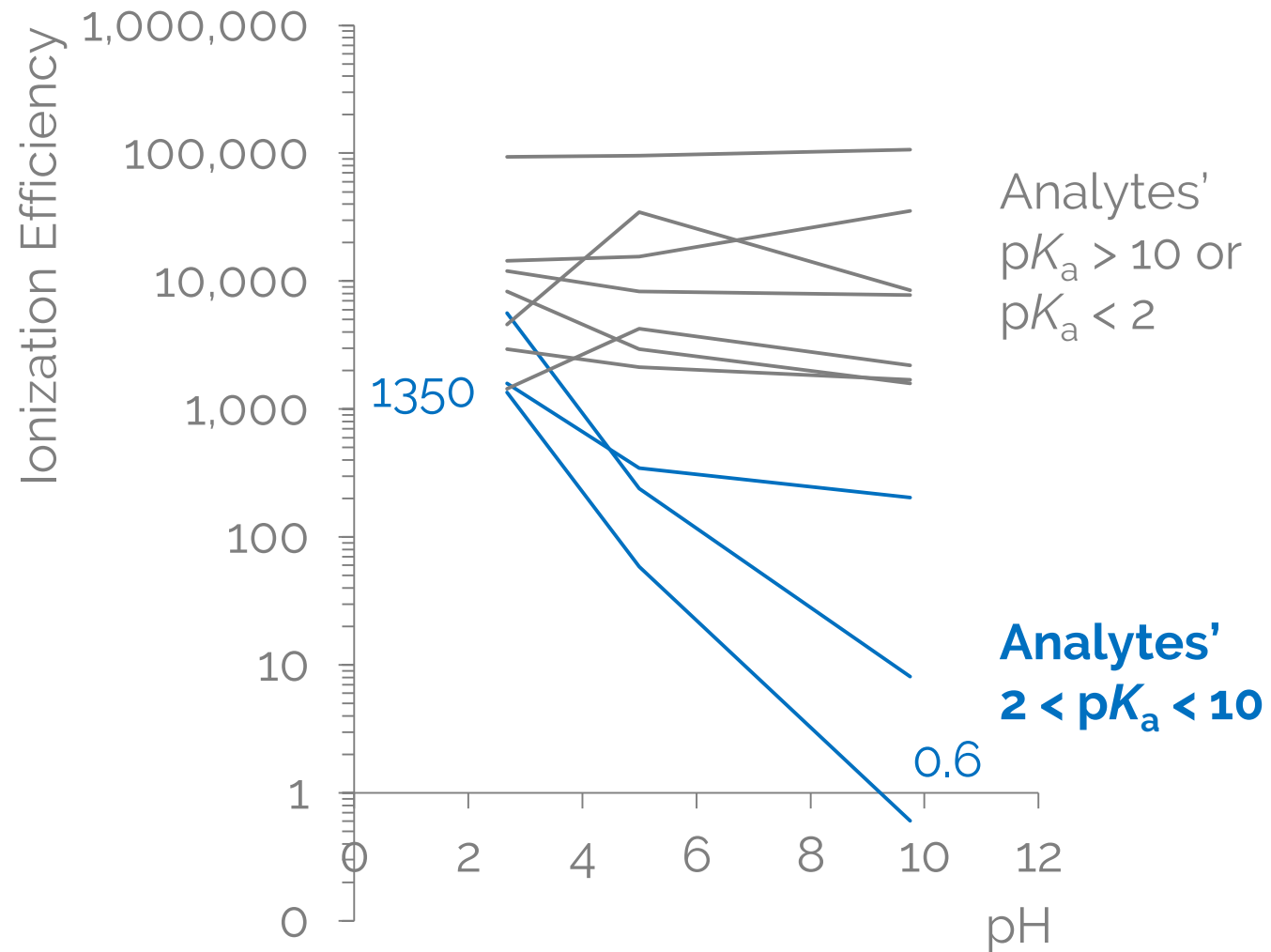
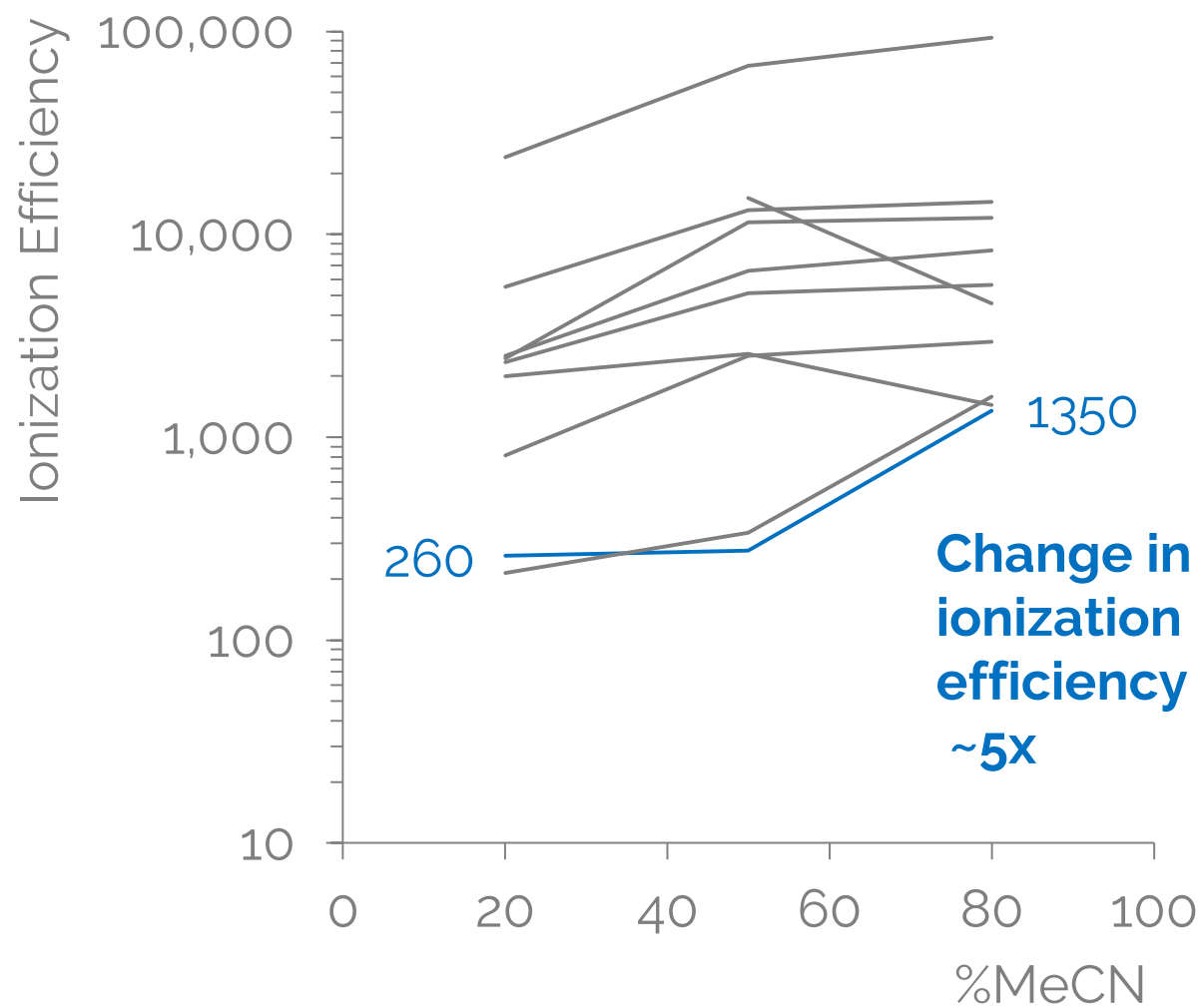
SOLVENT

ORGANIC SOLVENT CONTENT AND pH HAVE STRONG EFFECT ON IONIZATION EFFICIENCY



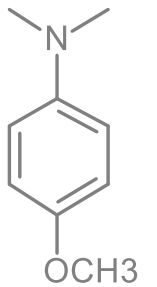
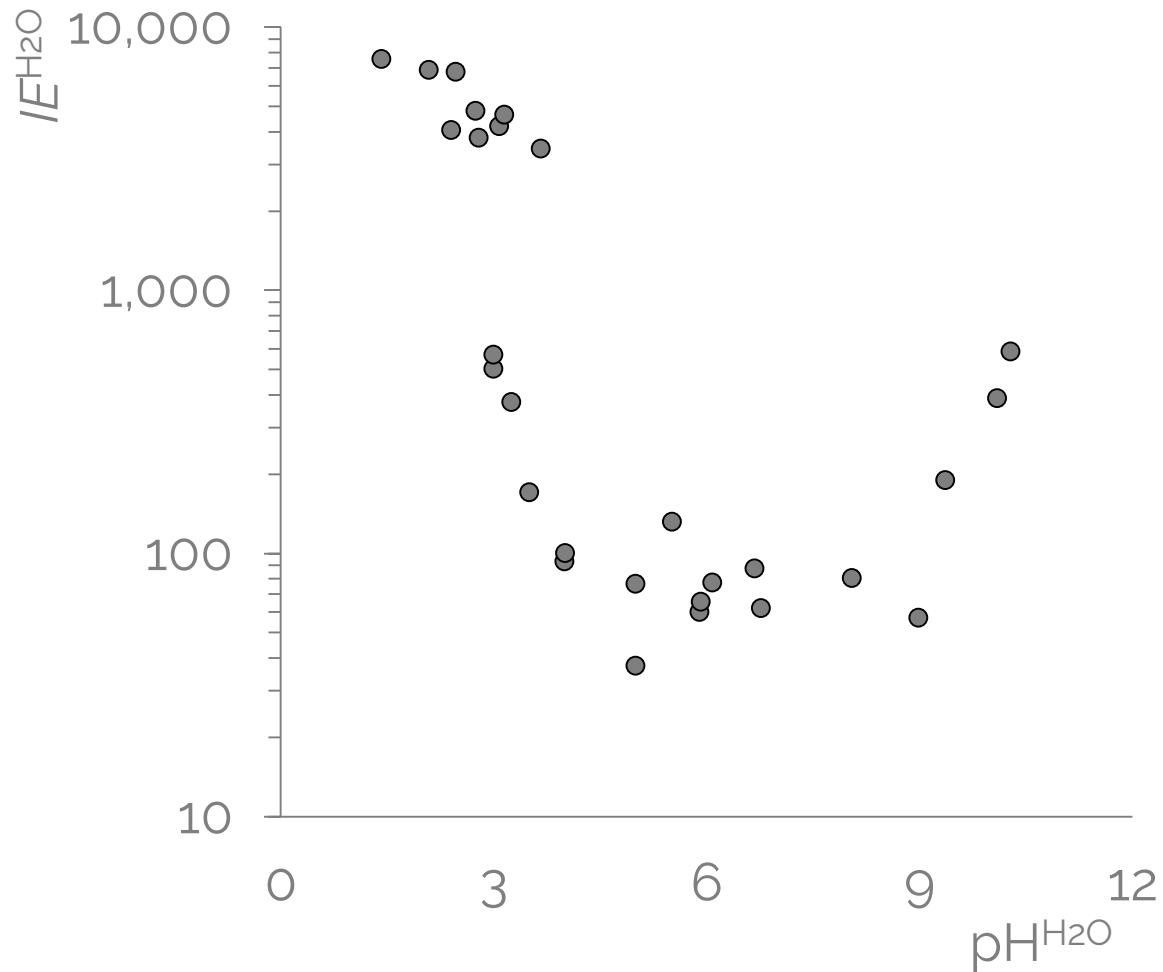
SOLVENT

ORGANIC SOLVENT CONTENT AND pH HAVE STRONG EFFECT ON IONIZATION EFFICIENCY



ADDITIVE EFFECT

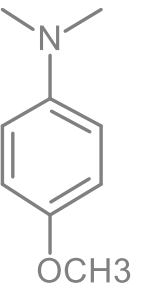
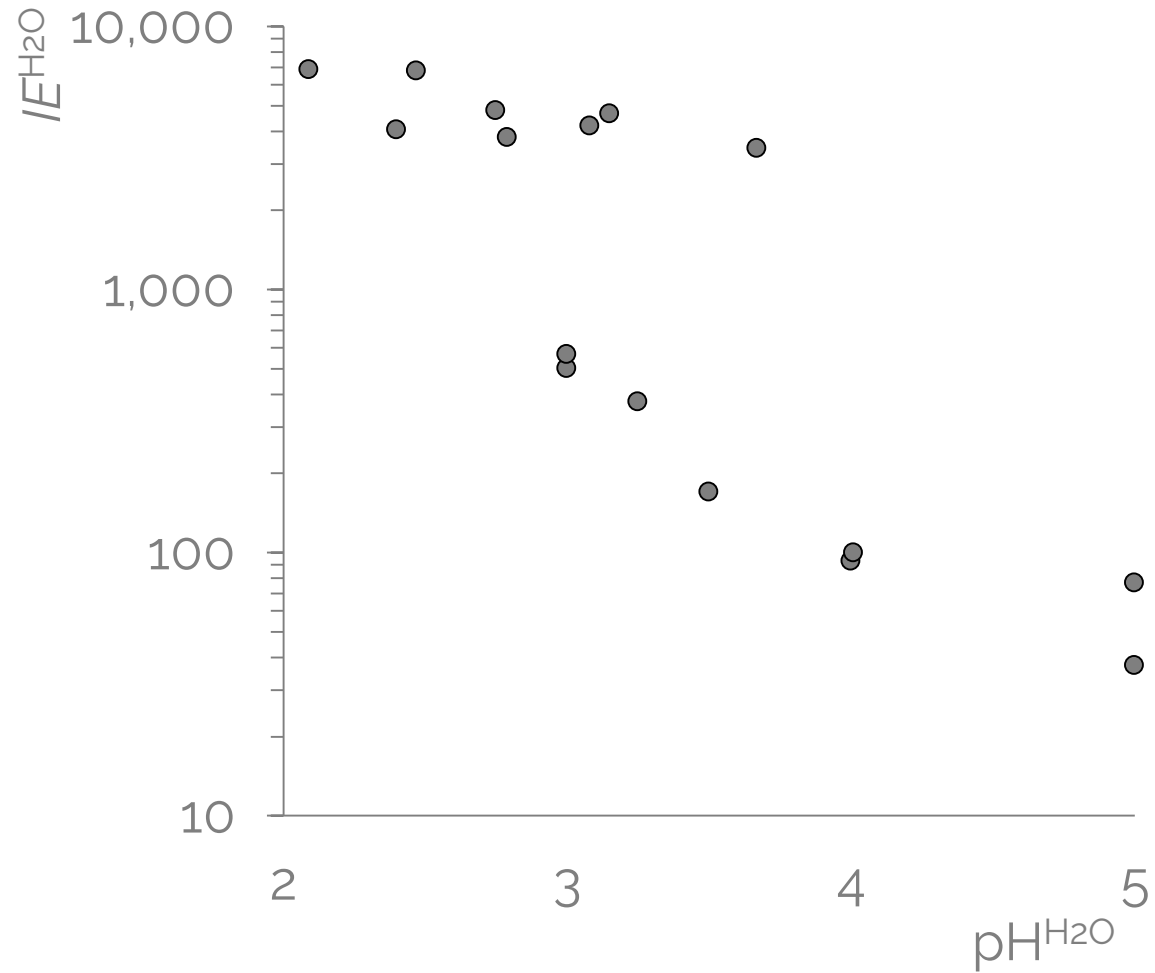
WATER DROPLETS



$$\text{p}K_{\text{a}}^{\text{H}_2\text{O}} = 5.8$$

ADDITIVE EFFECT

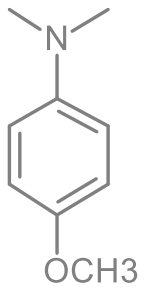
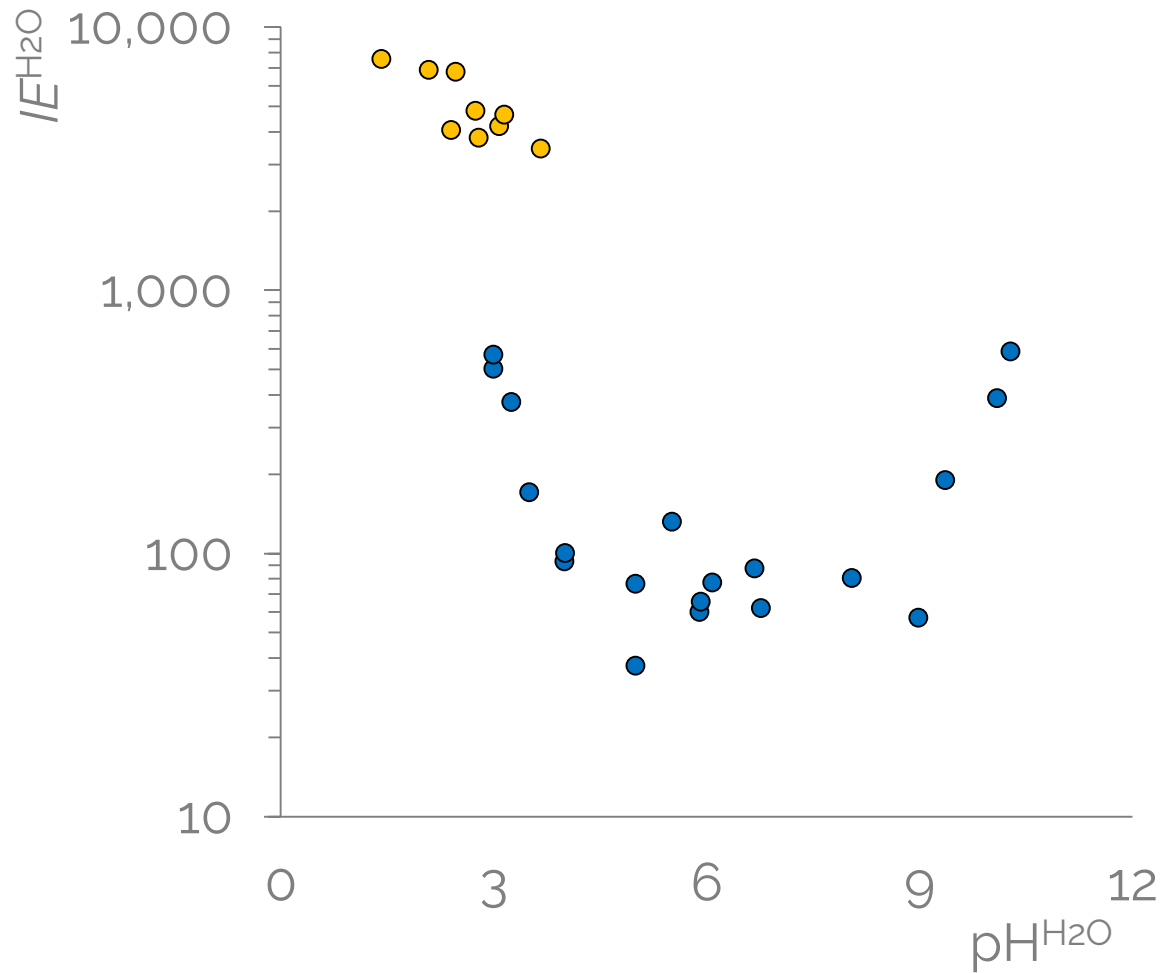
WATER DROPLETS



$pK_a^{H_2O} = 5.8$

ADDITIVE EFFECT

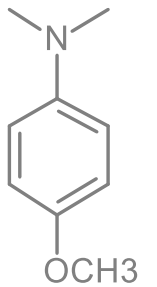
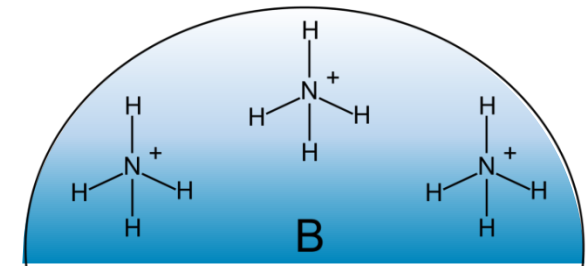
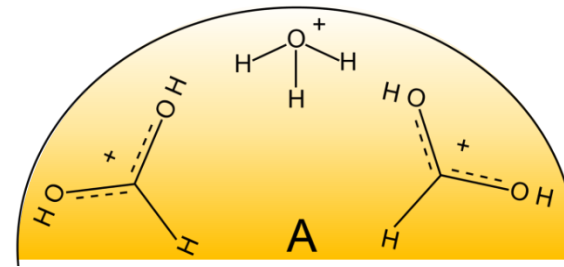
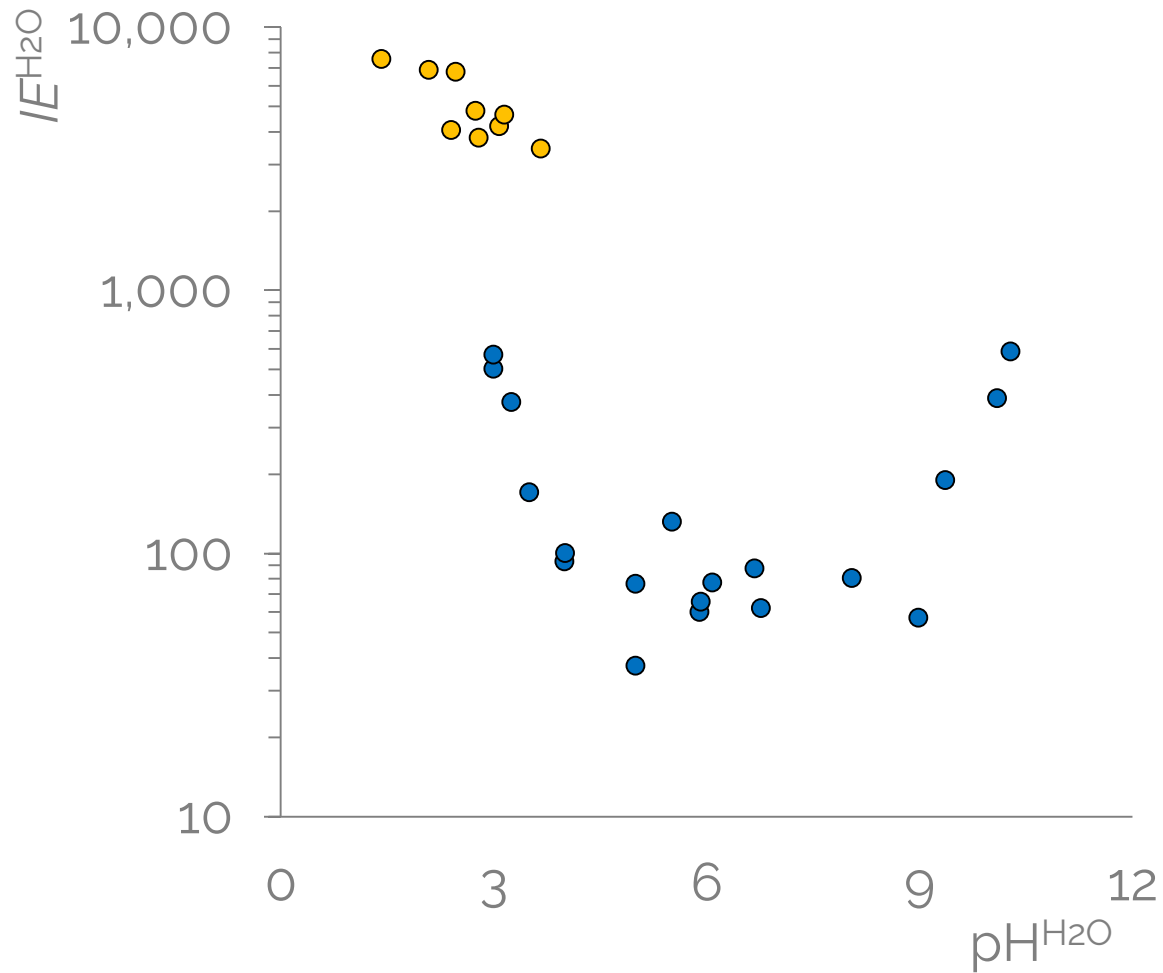
WATER DROPLETS



$$pK_a^{H_2O} = 5.8$$

ADDITIVE EFFECT

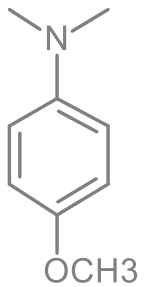
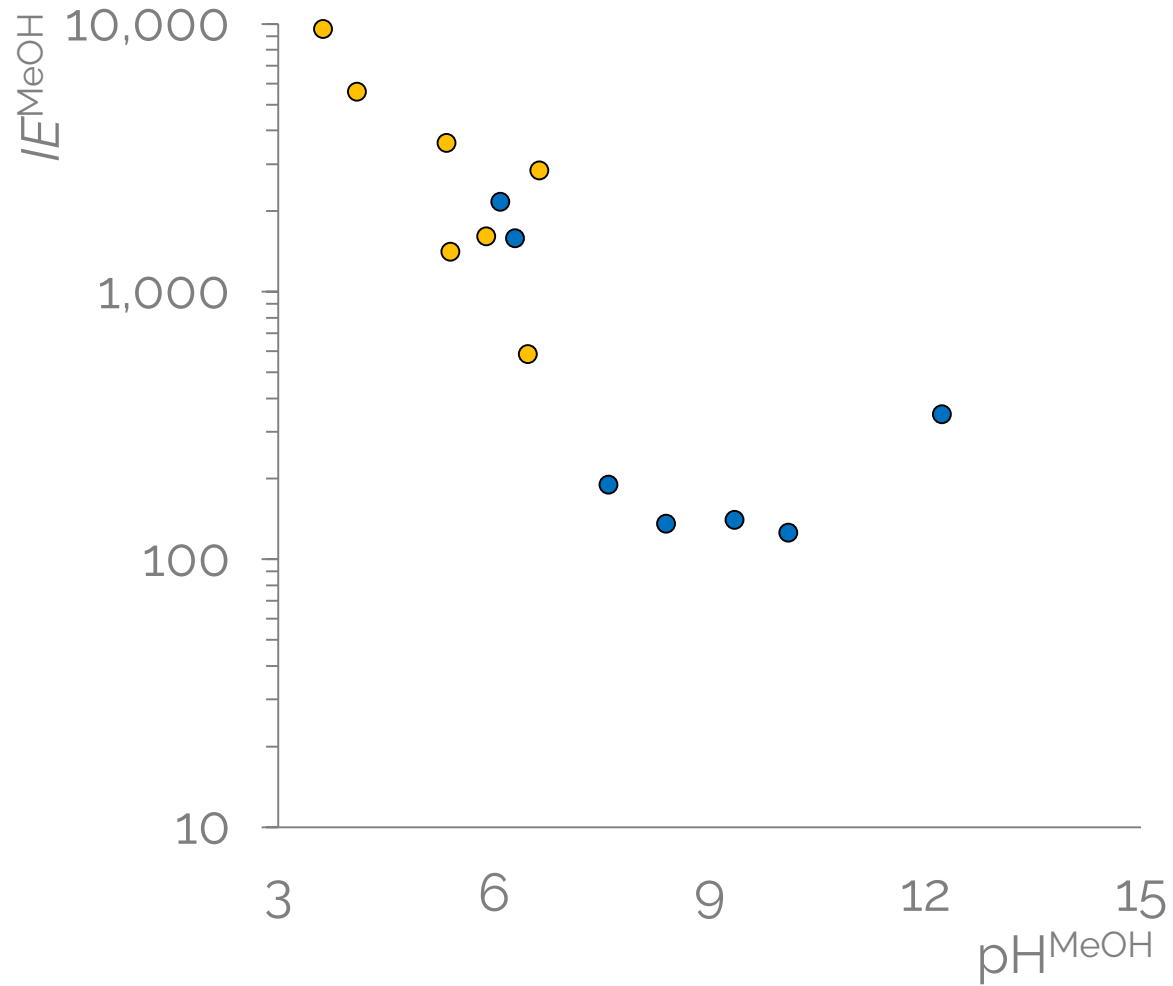
WATER DROPLETS



$$pK_a^{H_2O} = 5.8$$

ADDITIVE EFFECT

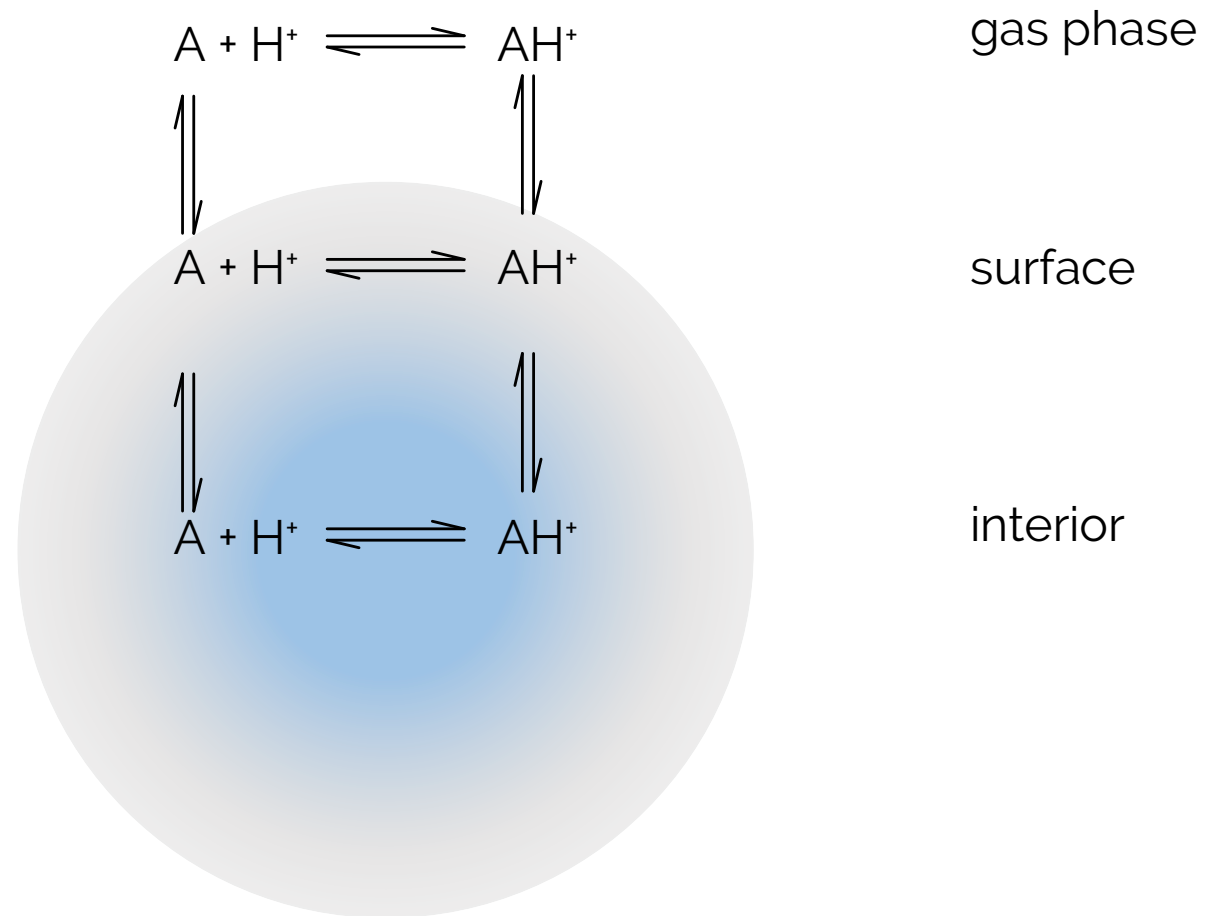
METHANOL DROPLETS



$$\text{p}K_{\text{a}}^{\text{H}_2\text{O}} = 5.8$$

UNDERSTANDING

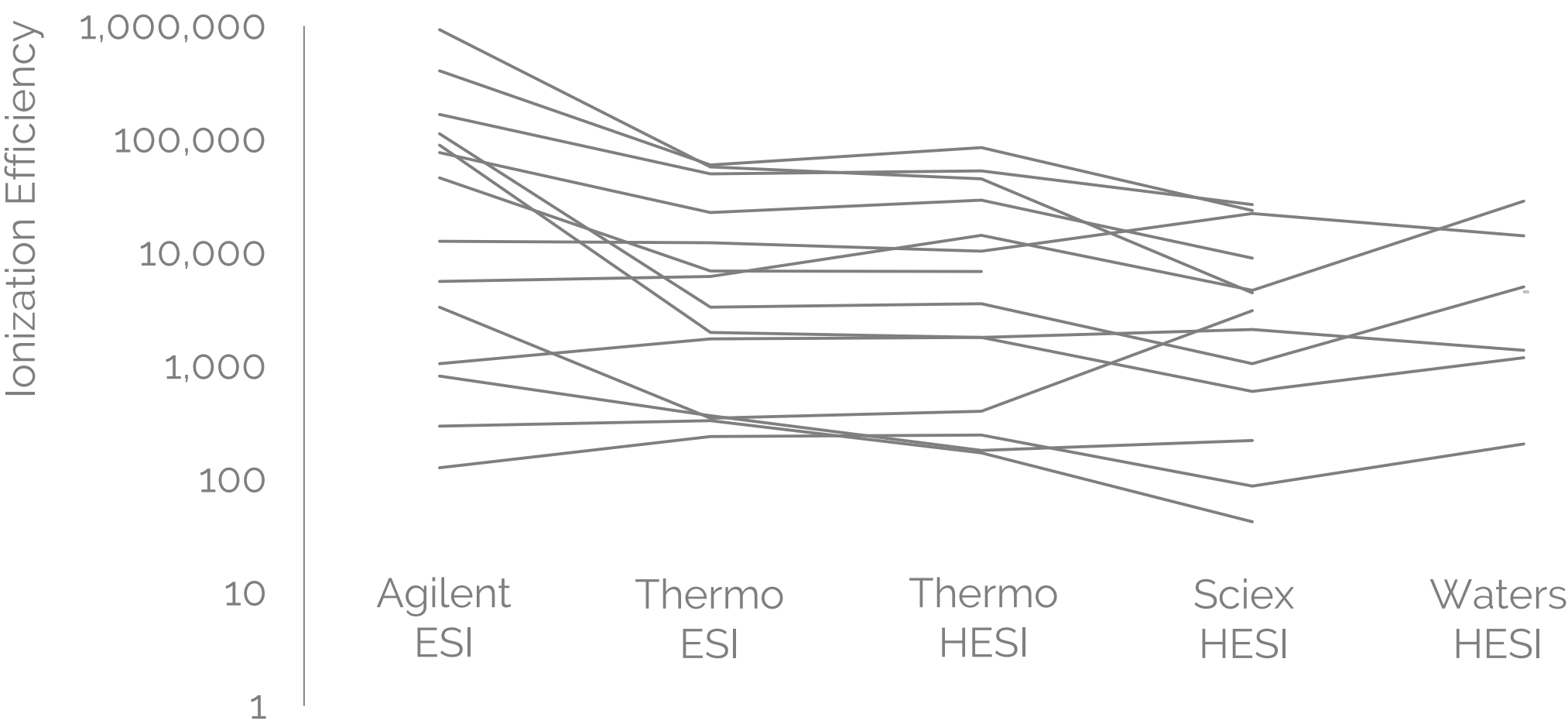
THE MECHANISM



INSTRUMENT

INFLUENCES IONIZATION EFFICIENCY

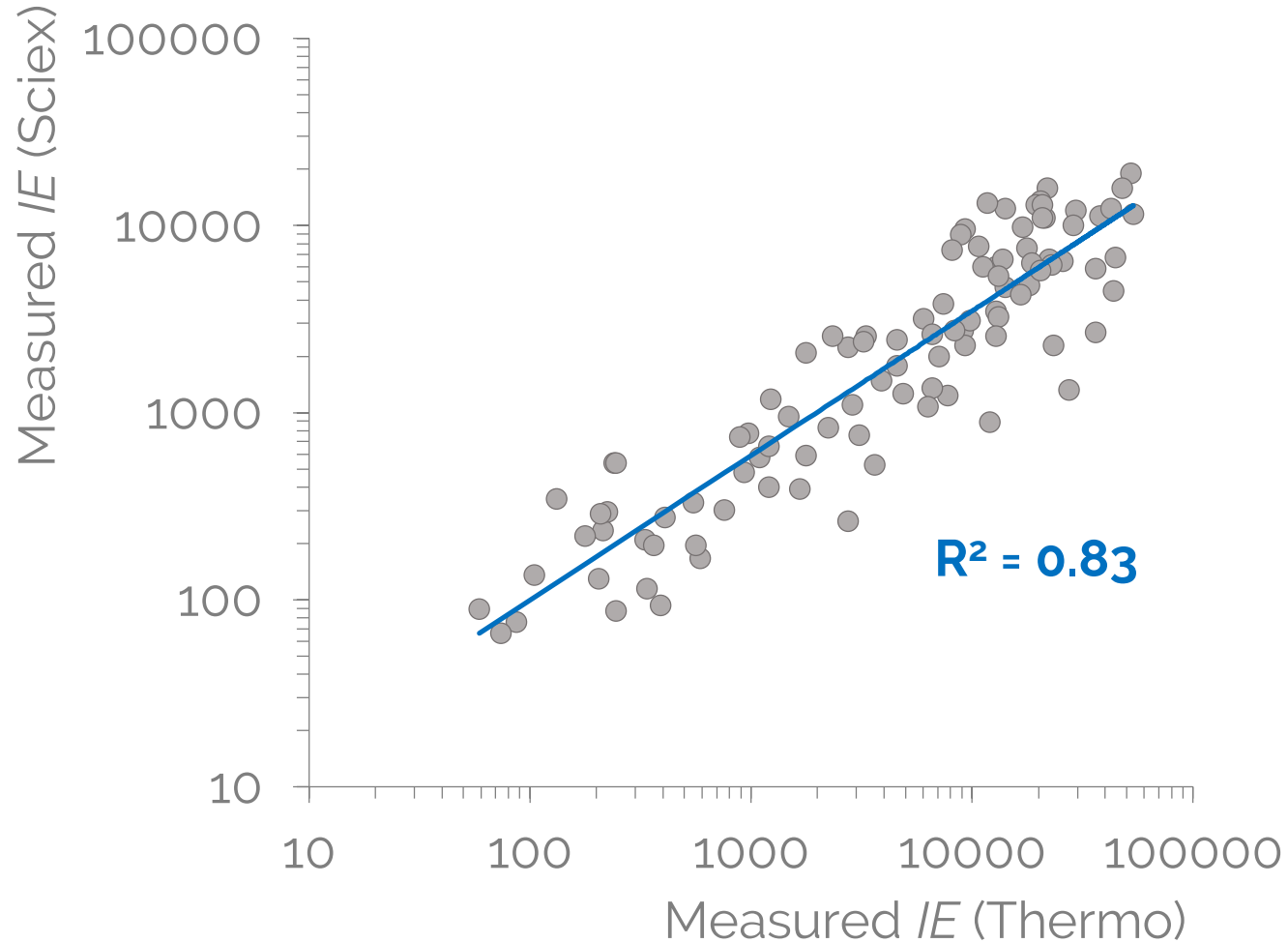
good correlation observed



INSTRUMENT

INFLUENCES IONIZATION EFFICIENCY

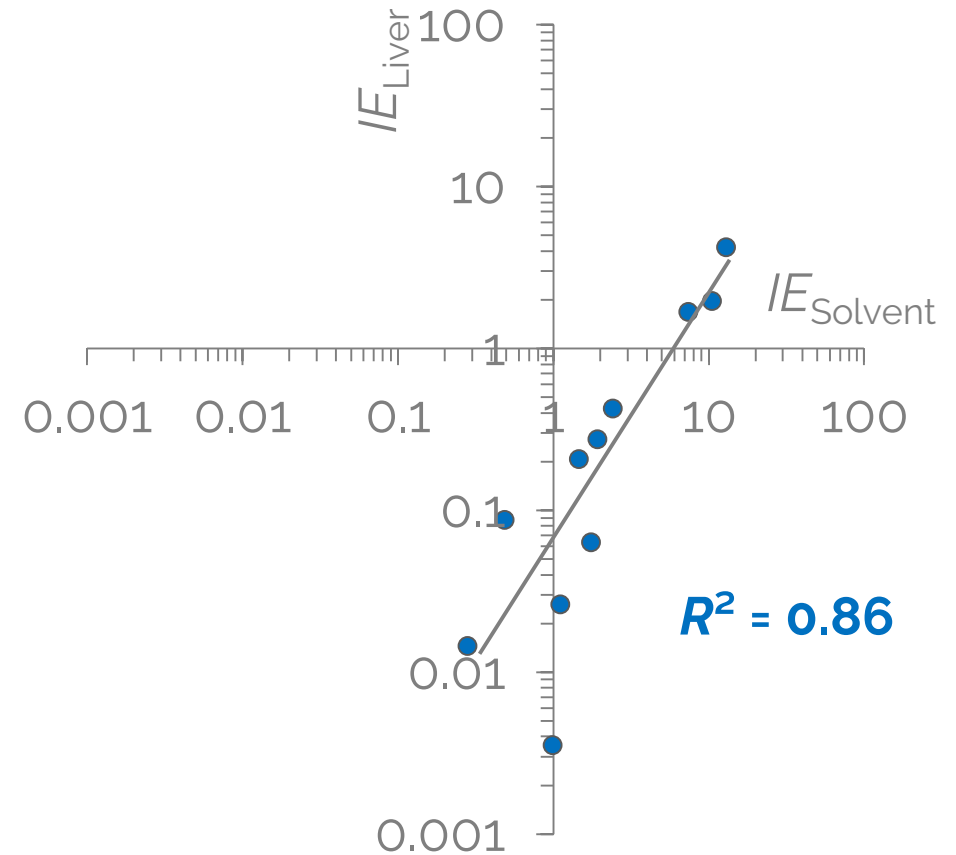
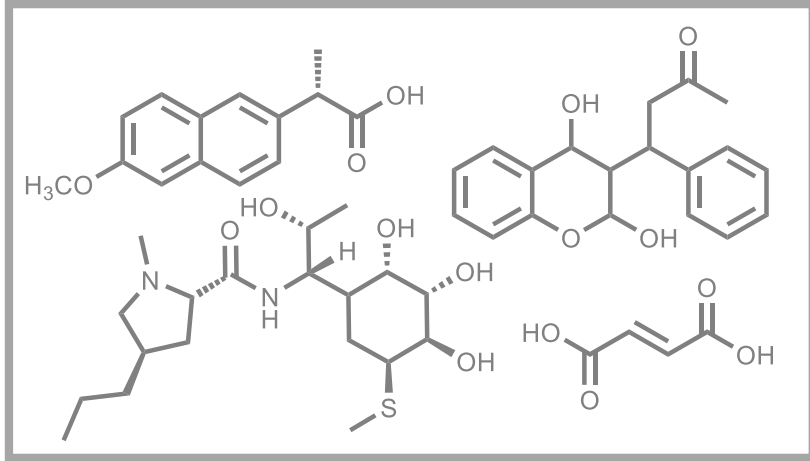
good correlation observed

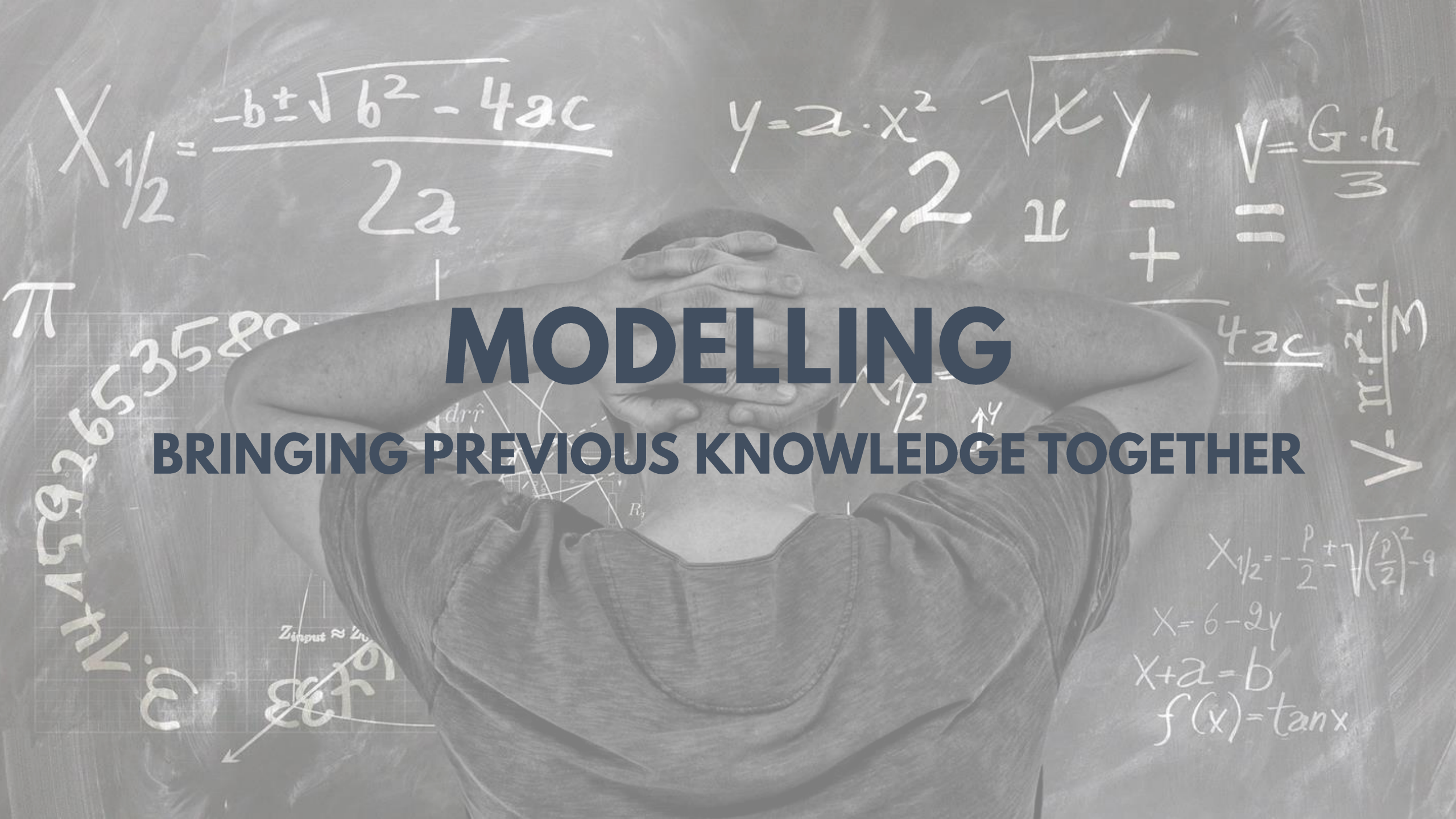


BIOLOGICAL MATRICES

SUPPRESS IONIZATION EFFICIENCY

good correlation with ionization efficiencies in solvent





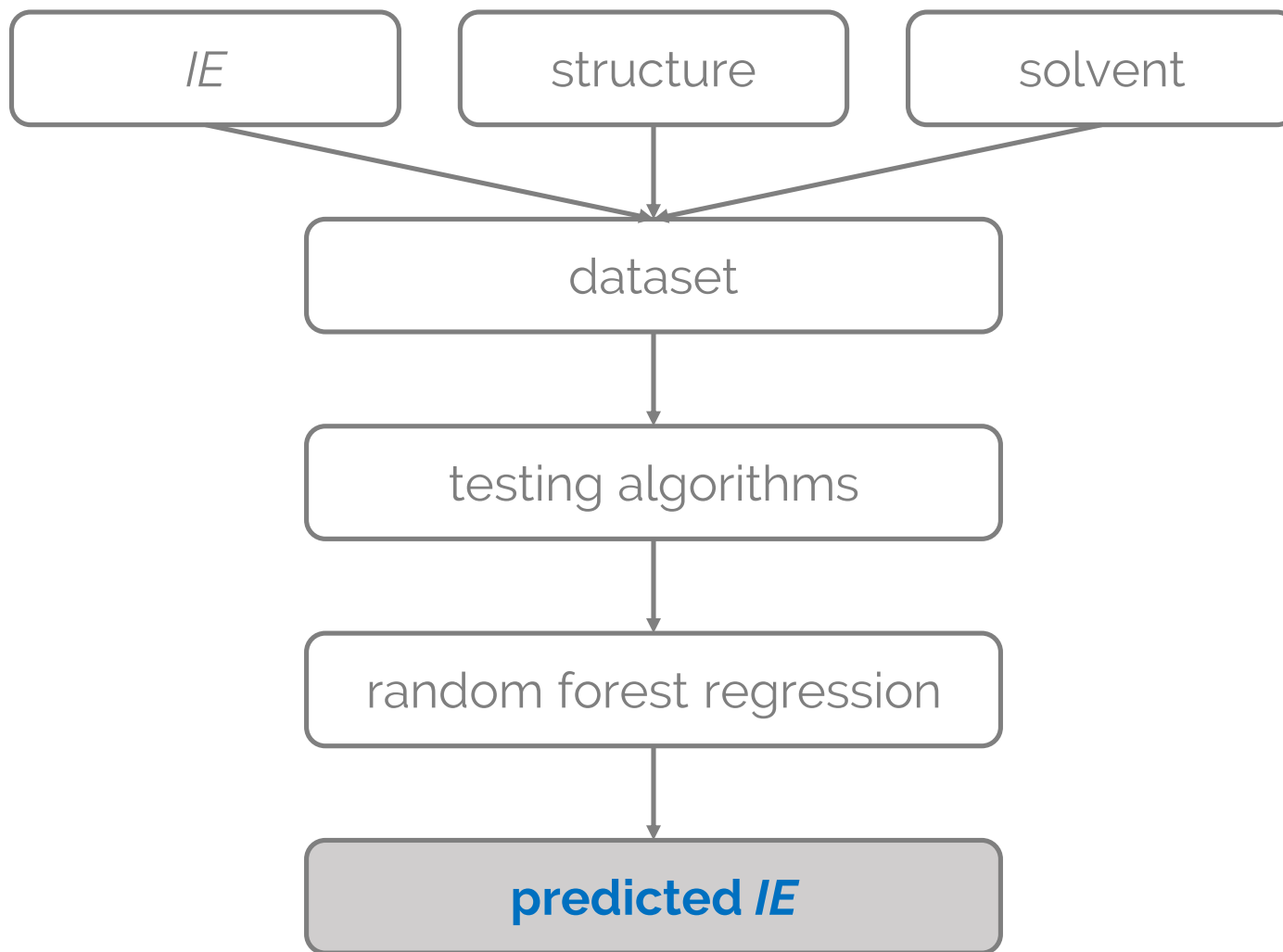
MODELLING

BRINGING PREVIOUS KNOWLEDGE TOGETHER

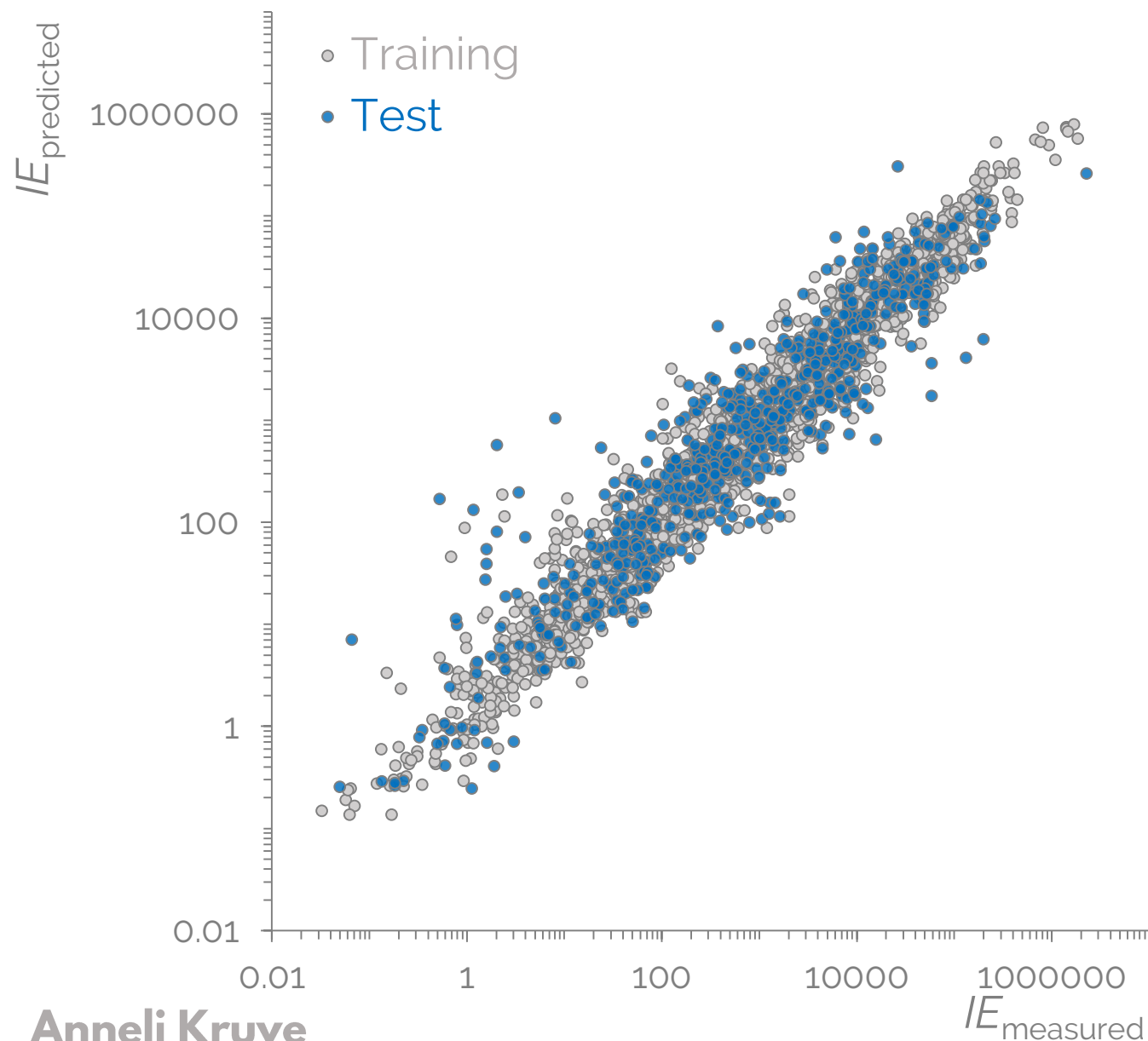
MACHINE LEARNING



MODELLING OF IONIZATION



PREDICTIONS IN ESI+



3139 data points

353 small molecules

106 eluent compositions

MeCN/MeOH

0 – 100%

pH = 2.0 – 10.7

Prediction error

Training set **1.9x**

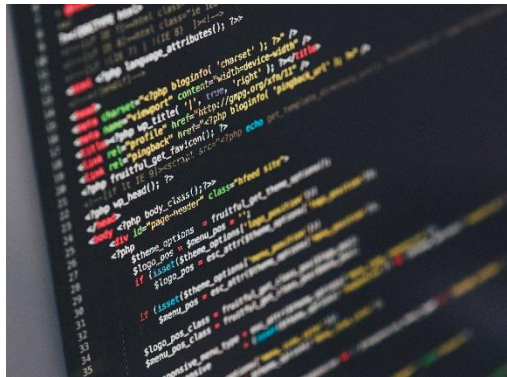
Test set **3.0x**

HOW TO USE IT?

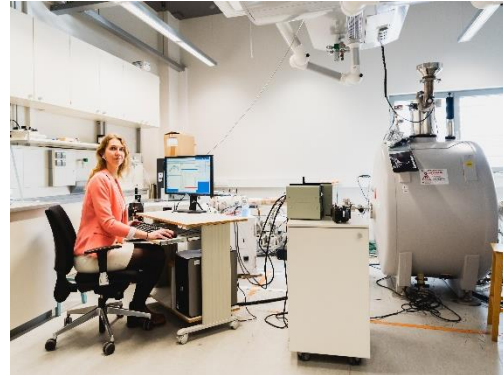
FOR QUANTIFICATION

in any given lab on any given instrument

predict



transfer



calculate





CONCENTRATIONS

PESTICIDES IN CEREALS

SAMPLES

PESTICIDES AND MYCOTOXINES

in oat, barley, rye, wheat, rice, maize

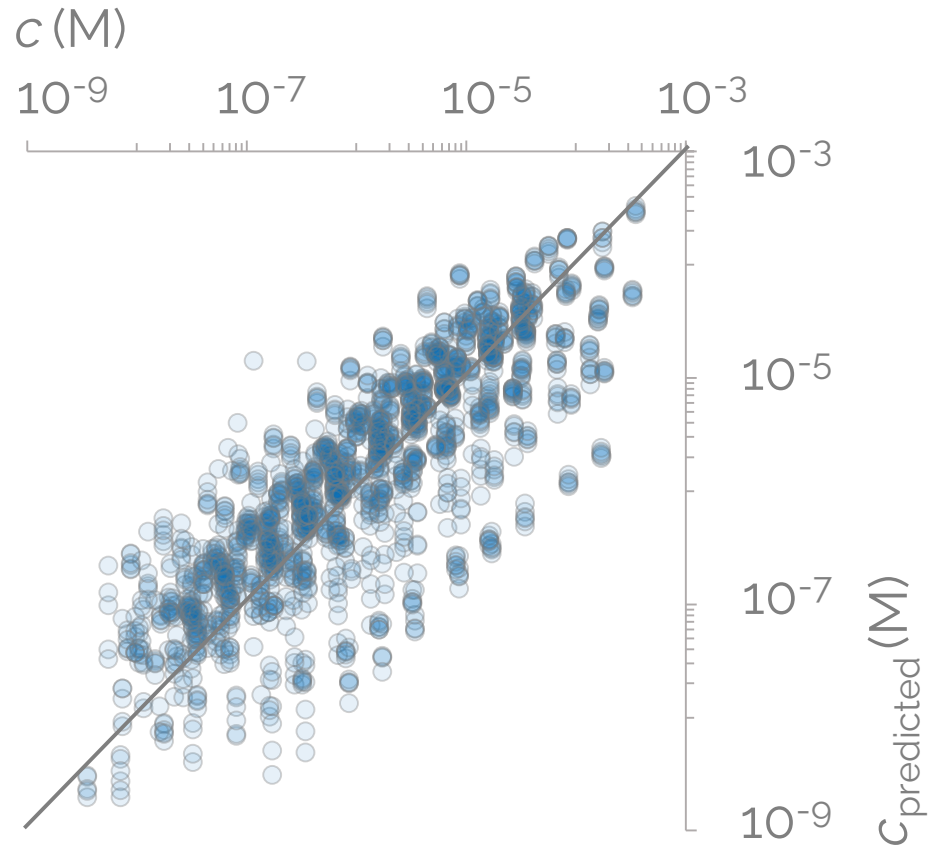


35 compounds + compounds with known concentration
concentrations 3.6 nM – 0.35 mM
measured on a QQQ

QUANTIFICATION

VALIDATION

for 35 pesticides in cereal samples



2233 data points

Mean prediction error 5.3x

89% of points with accuracy better than 10 fold

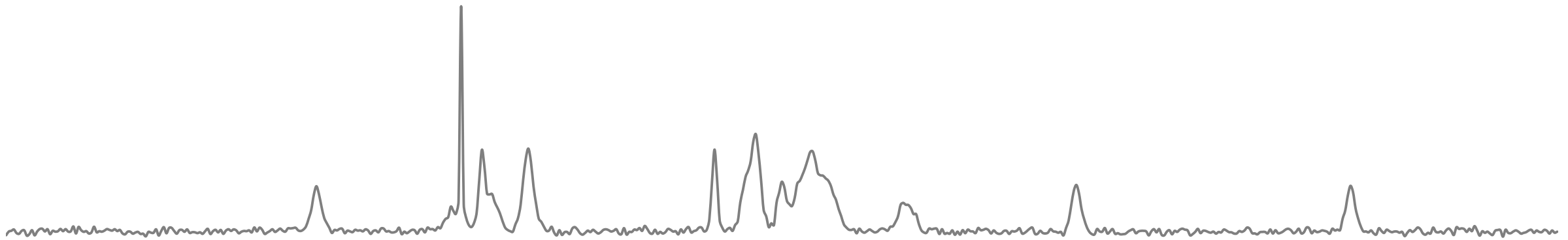
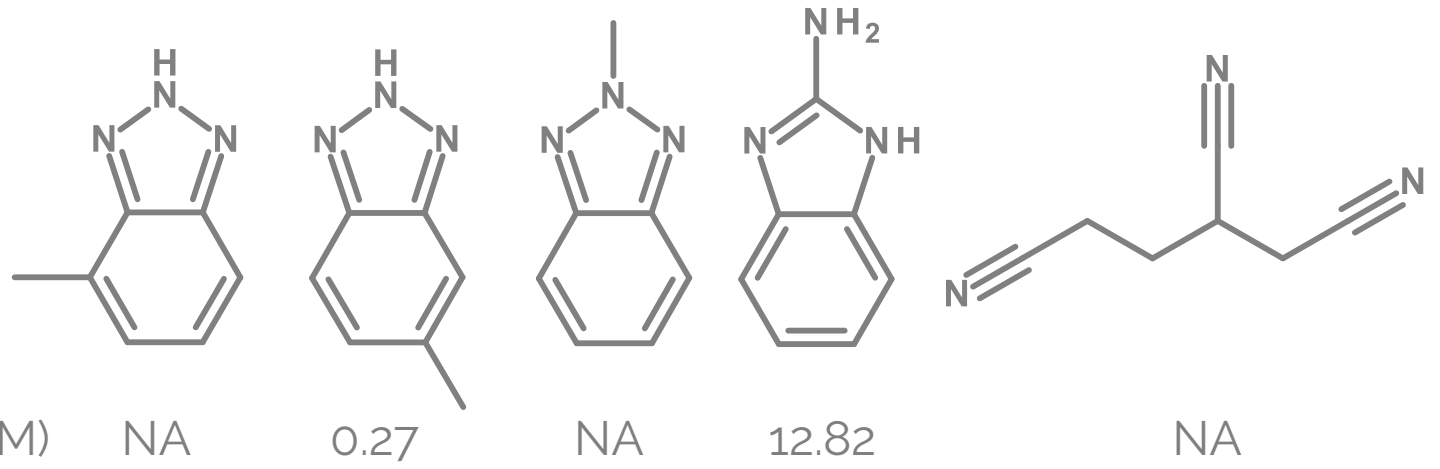
CONCENTRATIONS OF ENVIRONMENTAL CONTAMINANTS



PRIORITIZATION

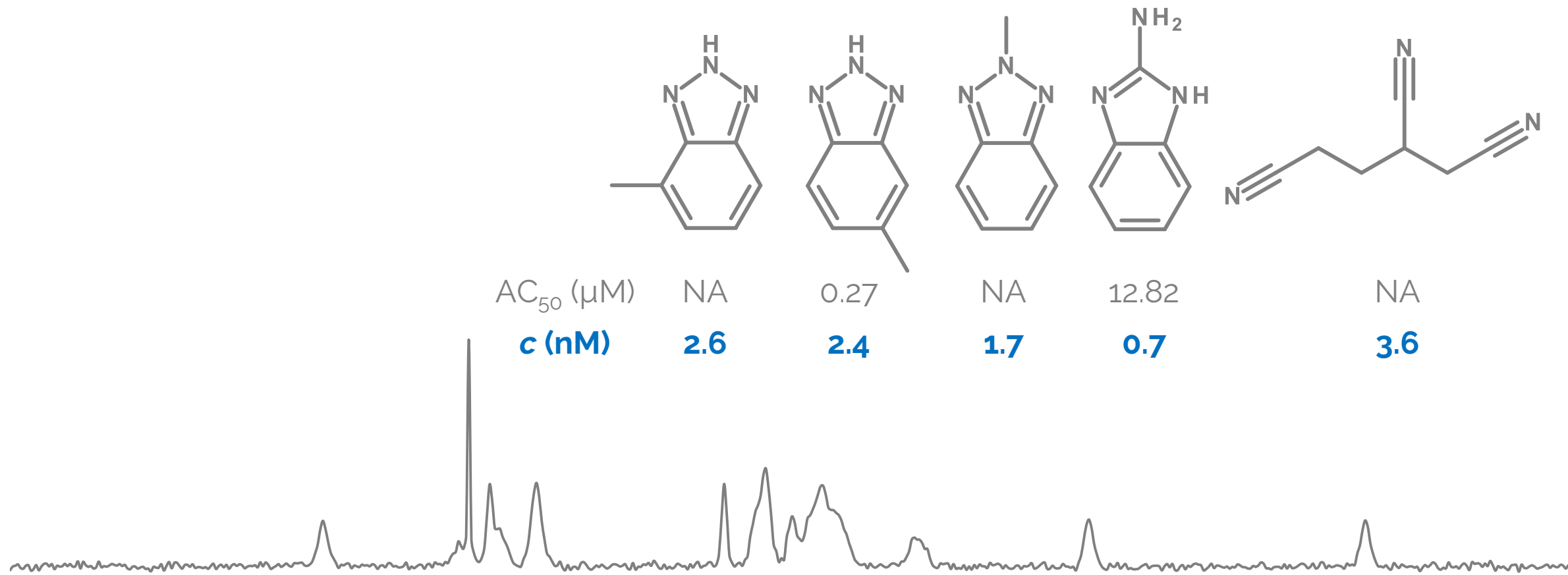
BASED ON TOXICITY

ToxCast toxicity tests

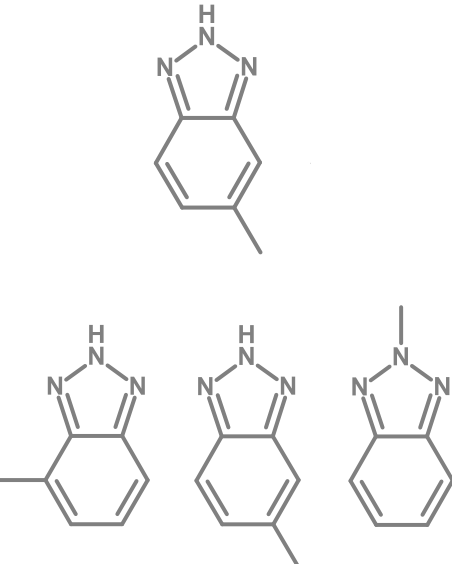


QUANTIFICATION

PREDICTED CONCENTRATION

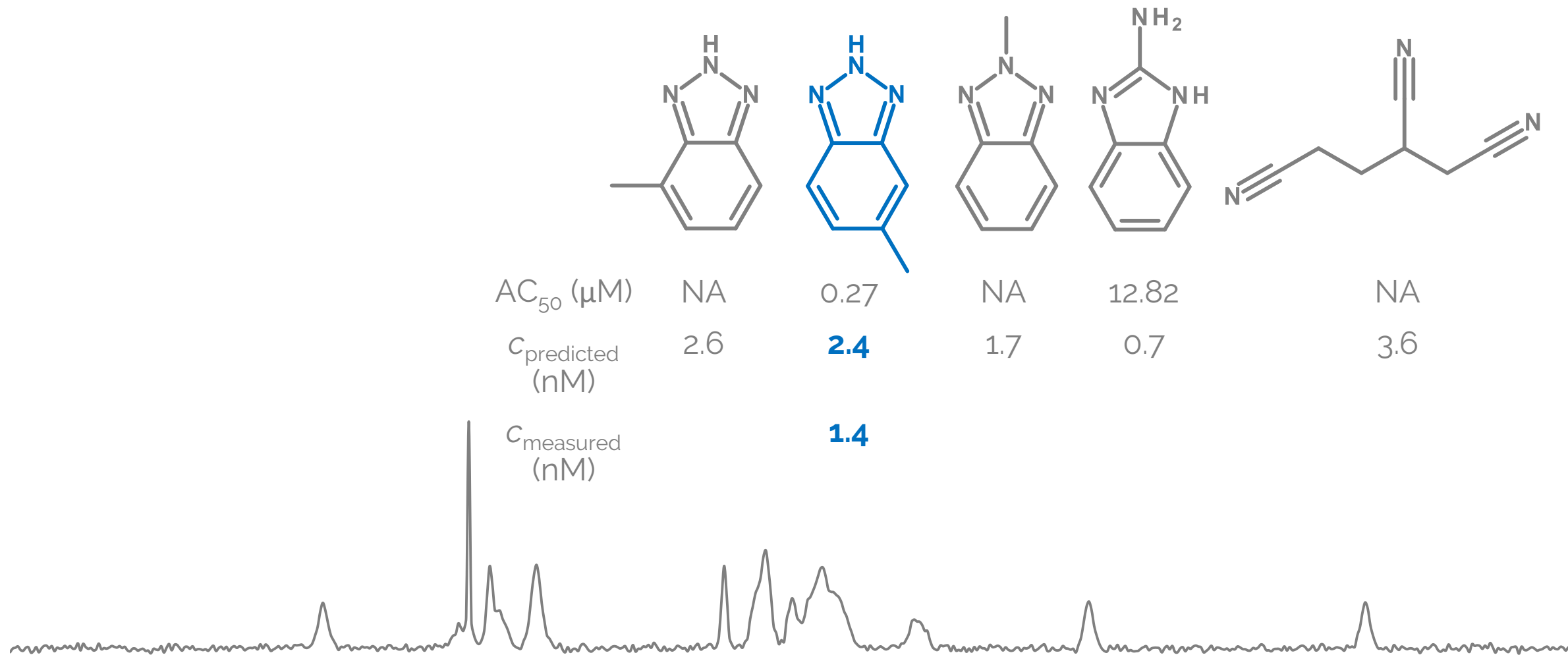


IDENTIFICATION LEVELS

Example	Identification confidence	Minimum data requirements
 <chem>Cc1ccc2nc[nH]c2c1</chem> <chem>Cc1ccc2n[nH]c2c1</chem> <chem>Cc1ccc2nc[n+](=O)c2c1</chem> $C_7H_7N_3$ 133.0640	Level 1: Confirmed structure by reference standard	MS, MS ² , RT, Reference Std.
	Level 2: Probable structure a) by library spectrum match b) by diagnostic evidence	MS, MS ² , Library MS ² MS, MS ² , Exp. data
	Level 3: Tentative candidate(s) structure, substituent, class	MS, MS ² , Exp. data
	Level 4: Unequivocal molecular formula	MS isotope/adduct
	Level 5: Exact mass of interest	MS

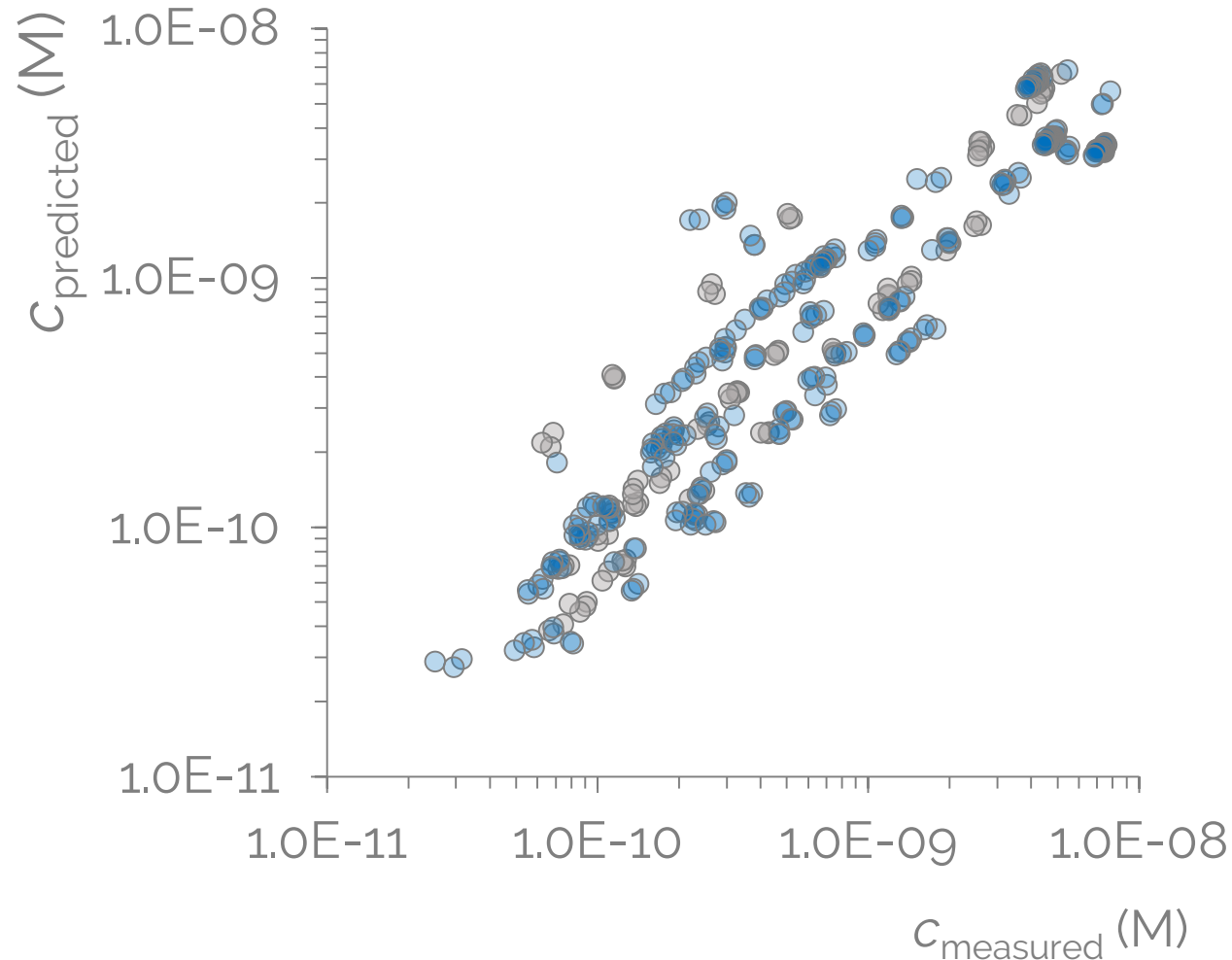
TARGETED METHODS

FOR CONFIRMATION AND QUANTIFICATION



QUNATIFICATION OF CONTAMINANTS

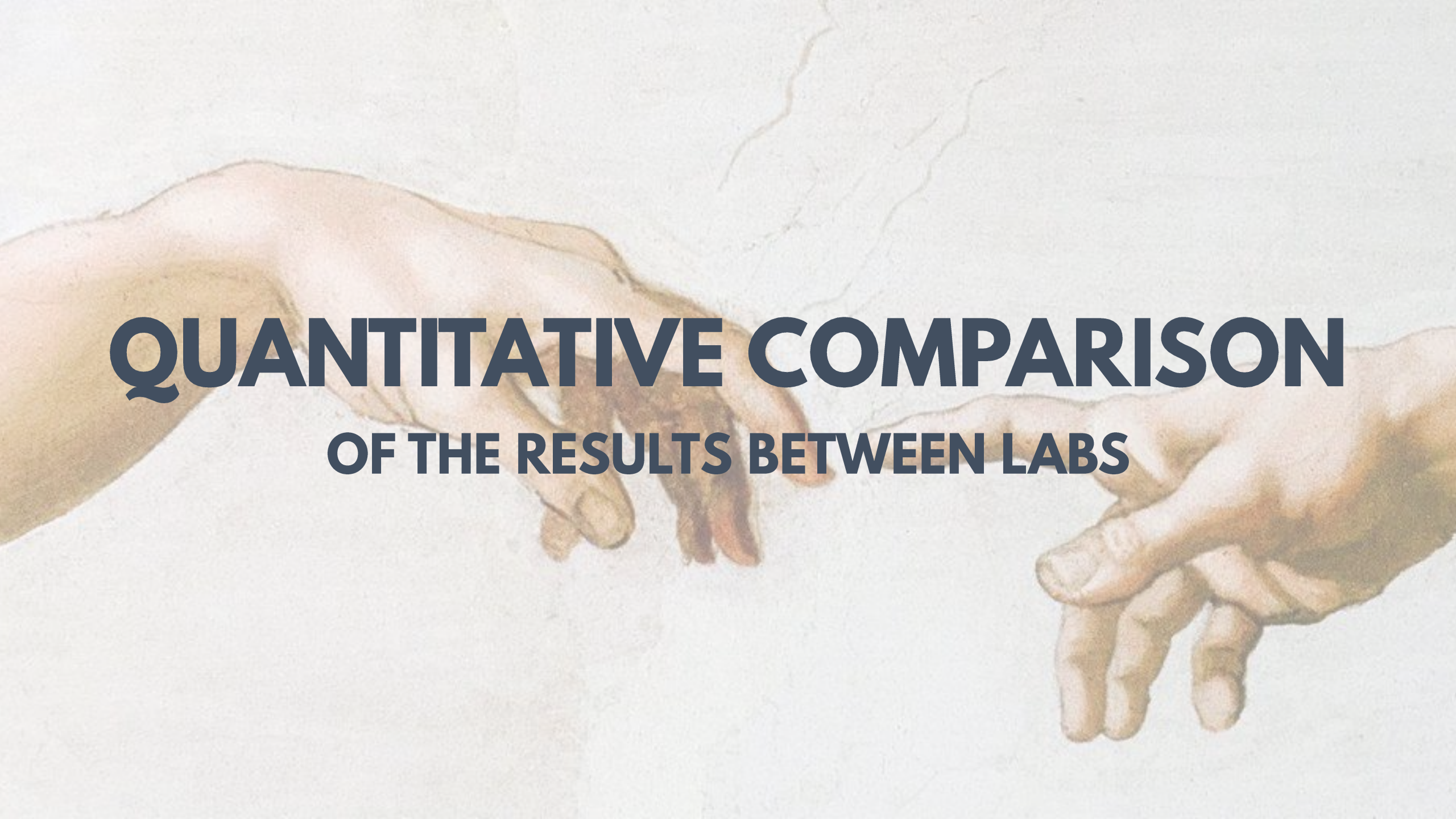
IN SURFACE WATER



28 contaminants from 28
surface water samples from
the Netherlands

Quantified with targeted
method

Mean prediction error **1.7x**

The background of the slide is a reproduction of Michelangelo's famous fresco, "The Creation of Adam," from the ceiling of the Sistine Chapel. It depicts two hands reaching toward each other, with the index finger of the hand on the right just inches from the index finger of the hand on the left. The text is overlaid on this image.

QUANTITATIVE COMPARISON

OF THE RESULTS BETWEEN LABS

INTERLABORATORY COMPARISON

134 PESTICIDES 6 CONCENTRATION LEVELS 6 CEREAL MATRICES



Testing Centre of University of Tartu
(Estonia)

4863 pesticides identified

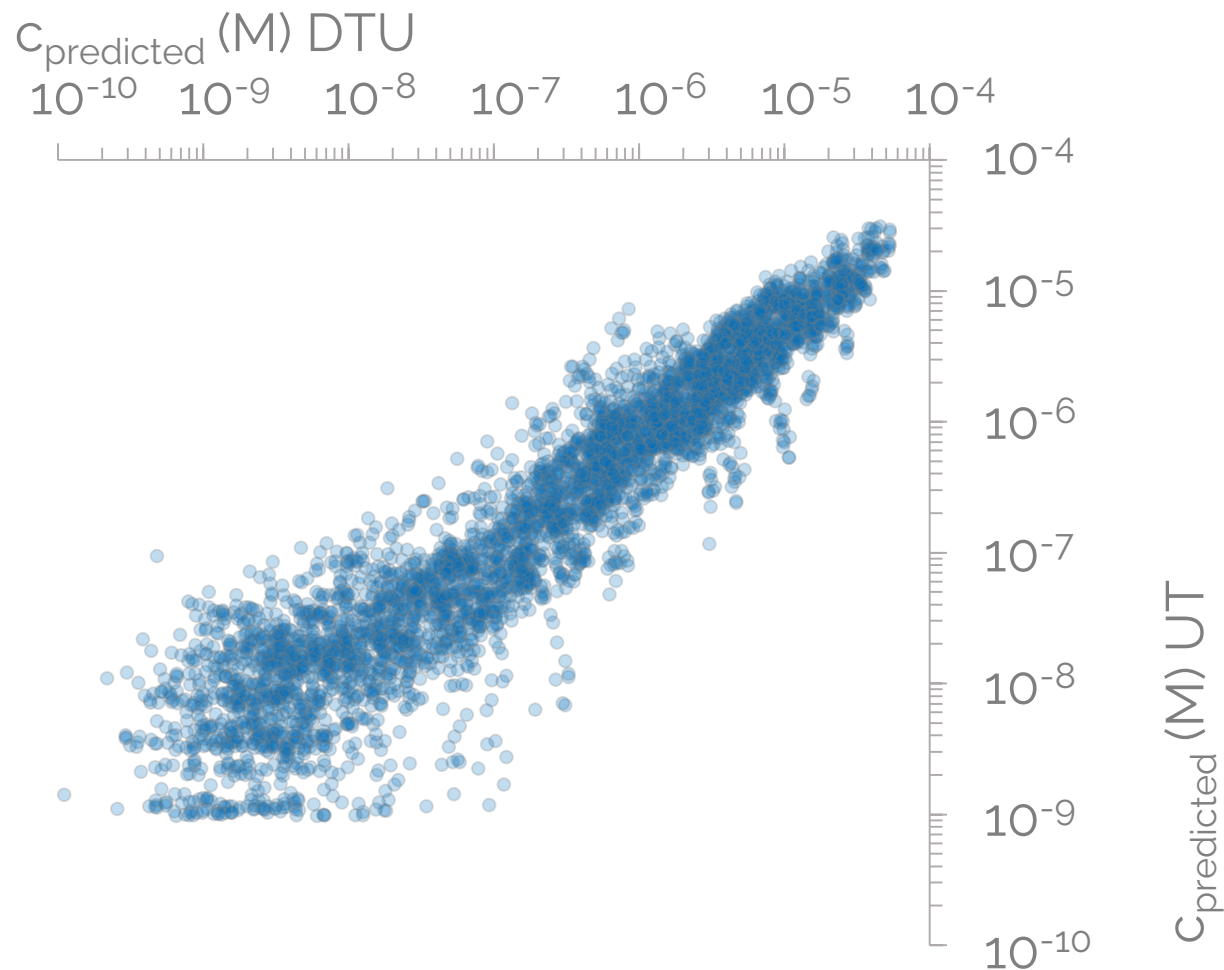


National Food Institute, Technical
University of Denmark

4907 pesticides identified

COMPARABILITY BETWEEN LABS

CAN BE ACHIEVED WITH STANDARD SUBSTANCE FREE QUANTIFICATION



4856 data points

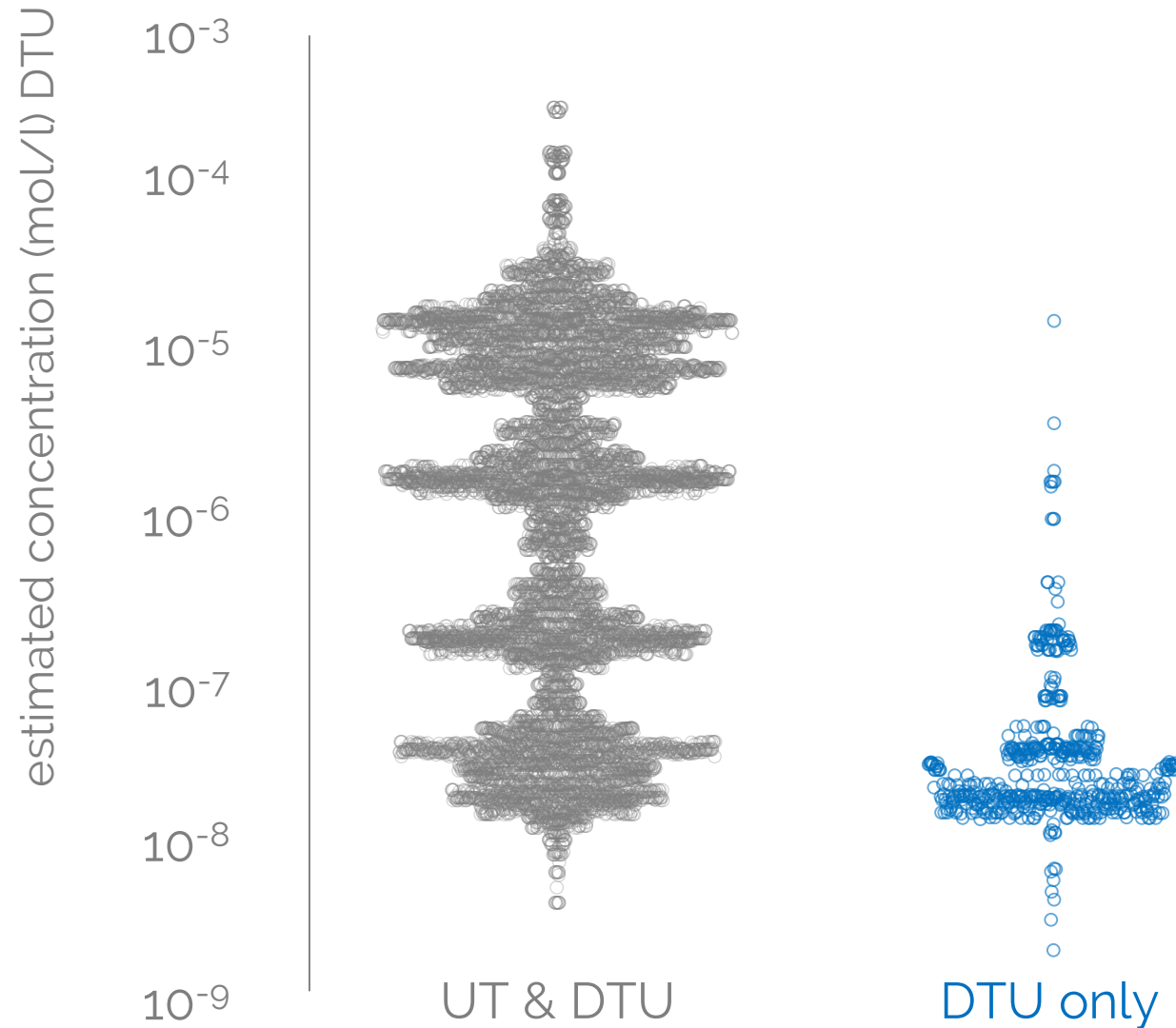
R^2 of 0.85

Average difference in concentration **3.2x**

89% of points with accuracy better than 10x

THE DIFFERENCES IN REPORTED PESTICIDES

RESULT PRIMARELY FROM DIFFERENT DETECTION LIMITS





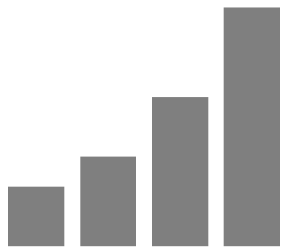
SUMMARY & FUTURE

OF THE COMPOUNDS DETECTED

FUTURE

FOR NON-TARGETED ANALYSIS

quantitative
results



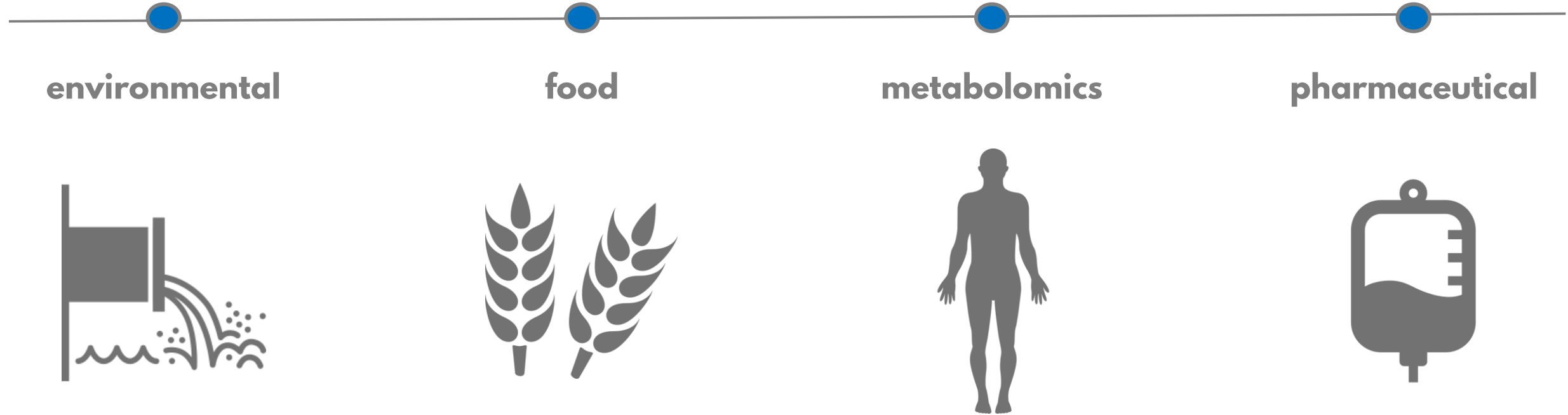
directly comparable
data from different
labs



retrospective
analysis



APPLICATION AREAS



OPEN POSITION

Post-doc in Computational Mass Spectrometry

A photograph of a modern laboratory with large windows in the background. Several scientists in white lab coats are working. In the foreground, a man is seated at a desk with two computer monitors, looking at one of them. In the background, other scientists are working at desks and using laboratory equipment. The text "OPEN POSITION" is overlaid in large, bold, dark blue letters.

OPEN POSITION

**Full Professor in Analytical Chemistry
in Stockholm University**



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